

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

EDITOR

Howard P. Doub, M.D.  
Detroit, Michigan



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JANUARY, 1954

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A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES  
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## Pancreatic, Ductal, and Vaterian Neoplasms: Their Roentgen Manifestations<sup>1</sup>

PHILIP J. HODES, M.D., EUGENE P. PENDERGRASS, M.D., and NORMAN J. WINSTON, M.D.<sup>2</sup>

THE SURGICAL treatment of tumors in the head of the pancreas, ampulla of Vater, and periampullary region has improved remarkably during the past decade. With this improvement has come new hope for patients with operable tumors in this region. It is essential, therefore, that radiologists familiarize themselves with the early roentgen manifestations of these neoplasms. To recognize them when they are large and seen with ease is not enough. Nor will it suffice to wait for jaundice before turning attention to this part of the upper intestinal tract. The best interest of the patient will be served only when radiologists develop a high index of suspicion with respect to these neoplasms. That this may lead to "over-reading" of roentgenograms and errors favoring disease when none actually exists is possible; that is the chance that must be taken if earlier diagnosis is to be encouraged. Before subjecting patients to exploration, all radiologic cunning and acumen must be exhausted. In early lesions even the surgeon often has difficulty in making the diagnosis at operation, and the most meticulous inspection and examination are required. Biopsy in this region being hazardous, it is essential that the radiologist be reasonably certain or have very strong suspicions that

the patient harbors the disease before making a diagnosis of a pancreatic tumor.

Being convinced that we were overlooking too many pancreatico-ampullary lesions, we decided to reinvestigate this entire problem. The records of everyone with a growth in the pancreaticoduodenal region including vaterian and common-duct neoplasms were reviewed. In all, the records of 105 patients were studied. In about one-half, the roentgenograms were available for study. Since carcinoma of the head of the pancreas, carcinoma of the ampulla and the papilla of Vater, and carcinoma of the common duct occasionally may not be differentiated from one another grossly or histopathologically, the data, herein presented, are subject to that error.

To summarize briefly, we failed to recognize about half of the tumors in this region, even though all were carefully studied with barium and some with air according to the technic of Engel and Lysholm (12). Beeler and Kirklin (1) reported a somewhat parallel experience. In only 50 of 108 patients with cancer in the head of the pancreas was the correct diagnosis made by radiologic studies. The remaining 58 examinations were considered negative.

Having completed the survey, we again

<sup>1</sup> From the Department of Radiology, Hospital of University of Pennsylvania, the Institutional Grant Program of the American Cancer Society, and the Penn Mutual Foundation for the Study of Neoplastic Disease.

<sup>2</sup> Trainee of the National Cancer Institute.

studied the roentgenograms originally misinterpreted. In almost every instance, the correct diagnosis could have been made from the original studies.

The purpose of the present report is to summarize the roentgen manifestations of carcinomatous lesions in the head of the pancreas, the ampulla and papilla of Vater, and the common duct. We regret that we have nothing new to report. The roentgen evidence of the above lesions has already appeared in the literature and is amply documented by Case (7), Poppel (29), and others (6, 11, 14, 16, 17, 19, 20, 30, 38). We will, however, re-emphasize and bring into focus what others have said, since we are convinced that this subject should be considered frequently, if radiologists are to assist in recognizing early lesions.

#### PATHOLOGY

It is not within the province of this report to discuss in detail the pathological characteristics of tumors arising in the pancreatico-ampullary region. Suffice it to say it is host to a wide variety of benign and malignant conditions (24, 39).

Bockus (2) classified malignant pancreatic tumors as carcinomas, sarcomas, carcinosarcomas, and malignant cysts, the sarcomas being mainly fibrosarcomas, angiosarcomas, and malignant lymphomas.

Of all pancreatic cancers, 65 to 85 per cent are reported to involve the head (1, 3, 9, 22). Usually scirrhus, gritty, and "rock-hard," the tumor varies considerably in size, the mean diameter being 4.2 cm. (1). Early infiltration of adjoining structures is characteristic.

The malignant tumors of the ampulla or papilla of Vater are far more common than the benign ones. Whereas Cattell and Pyrttek (8) feel they often arise from benign polyps, the latter have rarely been recognized radiographically. Smith and Blakemore (35) recorded such a case and found 21 additional examples in the literature, including papillomas, polyps, adenomas, lipomas, fibroneuromas, melanomas, and carcinoids.

As a rule, the malignant vaterian tumors are adenocarcinomas. Usually they grow slowly and are of low-grade malignancy, metastasizing late. They may be polypoid and protrude into the duodenum; they may appear ulcerated, with rolled edges. It should be re-emphasized that it may be impossible to distinguish between ampullary and papillary carcinomas or to differentiate them from the other neoplasms arising in this highly complex area (21, 22, 26, 28).

Common duct tumors also are more often malignant than benign. Among the benign tumors are lipomas, fibromas, adenomyofibromas, neuromas, and carcinoids. The malignant ductal tumors usually prove to be adenocarcinomas. Most common are the annular or nodular forms; villous and diffuse adenocarcinomas have also been described.

#### CLINICAL FINDINGS

The clinical history is of paramount importance in the recognition of pancreatico-ampullary disease. In many instances the history alone makes the diagnosis (2, 3, 9, 10, 22).

Carcinomas of the head of the pancreas are twice as common in women as in men. The average recorded age lies between fifty-six and fifty-eight years. Loss of weight and weakness are the common complaints during the pre-icteric stage. Coming on about three months before the onset of pain and six months before jaundice, these symptoms are highly significant. Usually weight loss, averaging almost 6 pounds per week, precedes the weakness. In most series, 85 per cent of patients give a history of loss of weight.

Pain is recorded as the initial symptom in almost 75 per cent of the cases. It may be dull and boring, arising in the epigastrium and radiating to the back; it may be peri-umbilical and paroxysmal, radiating widely throughout the back, chest, and abdomen; or it may be colicky, starting in the right hypochondrium and then radiating into the right subscapular region.



Almost 33 per cent of patients with cancer of the head of the pancreas list jaundice as their initial complaint. Eventually about 90 per cent become icteric. Painless jaundice occurs in from 25 to 40 per cent. It is noteworthy that when patients complain of pain plus jaundice, the jaundice usually follows the pain. Among other symptoms are diarrhea, anorexia, vomiting, nausea, and easy fatigability. From 60 to 75 per cent of the patients show an enlarged liver and about one-half present distended gallbladders.

The malignant vaterian tumors are found slightly earlier in life than those of the pancreas, closer to fifty than to fifty-eight years. The chief complaints include upper abdominal or epigastric pain, obstructive jaundice, weight loss, anemia, anorexia, vomiting, and diarrhea. Jaundice is outstanding and occurs in about 90 per cent of the cases. According to Brunschwig and Templeton (5), obstructive jaundice associated with early pain and subsequent disappearance of the pain are characteristic of vaterian tumors.

With infiltration and erosion of mucous membranes, bleeding and secondary anemia ensue. Whereas pain usually heralds the onset of pancreatic cancer, in the vaterian neoplasms painless jaundice and anorexia are more common. It is noteworthy that the duration of weakness as a major complaint occurs far less often in vaterian tumors than in the pancreatic group. In the former, weakness averages about eleven weeks in duration; in pancreatic cancers, it approaches nine months.

Vomiting also occurs much more commonly (about 40 per cent) in tumors of the ampulla and papilla of Vater. It is often associated with pain, increasing jaundice, chills and fever. Hepatomegaly and a palpable gallbladder complete the picture, occurring a little less often in the vaterian group than in the pancreatic lesions.

According to the literature, common duct cancers usually occur in males. In

our own series of 9 patients, 5 were men. Progressive obstructive jaundice, pruritus, and epigastric pain are the cardinal clinical complaints. As a group the clinical findings in patients with cancer of the common duct parallel those of pancreatic and vaterian origin.

It is noteworthy that in patients with pancreatico-ampullary carcinoma, as in those with bronchogenic carcinoma, venous thrombosis often develops.

According to Neeffe (25), a combination of the following laboratory tests must be viewed with a great deal of respect when tumors in the head of the pancreas are suspected: occult blood in the stools, obstructive jaundice, and a moderately elevated blood amylase or lipase. As a rule, liver function tests are not obtained soon enough in patients with jaundice to establish a reliable base line early. Too often the tests are done late, when the obstructive features of the disease have become complicated by hepatitis. Usually in obstructive jaundice the flocculation tests are negative, the alkaline phosphatase is elevated, and the total cholesterol is high. When hepatitis develops in patients with obstructive jaundice, the laboratory tests veer toward those found in primary hepatic jaundice, with the flocculation tests becoming positive and the phosphatase and cholesterol determinations approaching the normal or but slightly elevated.

#### ROENTGEN MANIFESTATIONS

Pancreatico-ampullary tumors often cannot be differentiated from one another by radiologic means. This is to be expected since, involving either the head of the pancreas, ampulla, papilla, common duct, or duodenum, all occur relatively close together. Yet early lesions can occasionally be distinguished by roentgenologic means, particularly the vaterian tumors. These latter infiltrate the immediate environs of the ampulla and produce localized mucosal changes in the duodenum that sometimes are distinctive (Fig. 1). Primary duodenal neoplasms are more apt

to be identified radiographically, particularly those arising in the lateral wall (Fig. 2). As a rule, however, all tumors in this area look alike. In all there is a "mass" which causes distortion. All "infiltrate" adjoining viscera and cause changes in the mucosal pattern. Because

(1) showed this, and our experience has been similar with tumors 10 cm. or less in diameter. The fact that strategically placed tumors cause early visceral distortion also militates against subdivision into stages.

The recognition of tumors of the head of

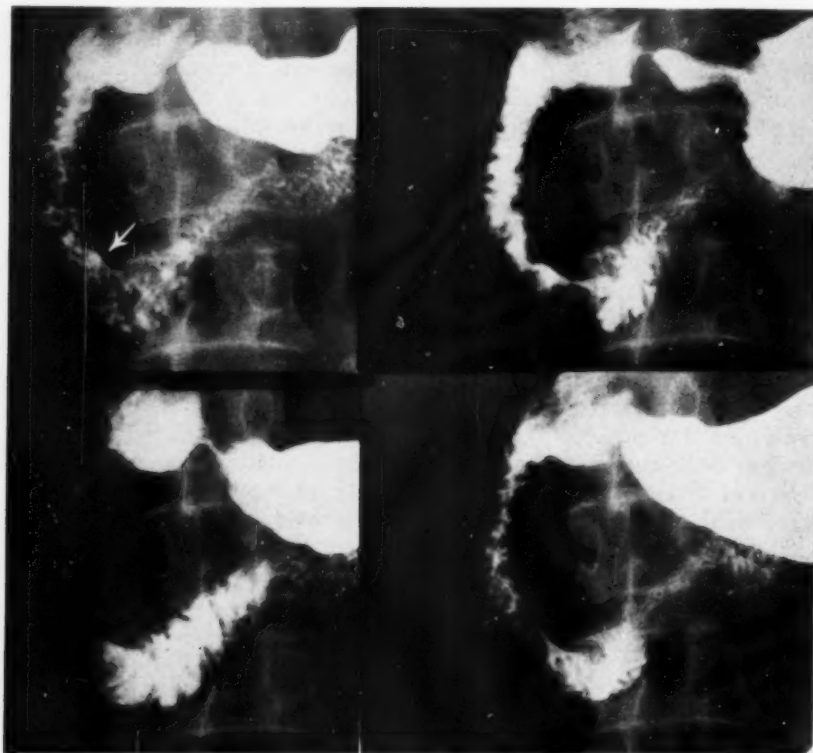


Fig. 1. Carcinoma of common duct. Patient 58 years of age complained of chills, fever, nausea, and vomiting of five years duration. She was jaundiced. At operation a carcinoma of the common duct was found secondarily invading the head of the pancreas. The arrow in this serial group of films points to the zonal irritability and altered pattern that characterize these tumors when they invade the duodenum.

of this, no effort will be made to treat each group of tumors separately. The following discussion applies to the entire group of pancreatico-ampullary neoplasms.

One is tempted to divide the roentgen manifestations of these cancers into three stages, the early, intermediate, and late. Apparently, however, there exists no significant relation between the size of the tumors and their ease of demonstration by roentgen technics. Beeler and Kirklín

the pancreas, ampulla and papilla of Vater, and common duct, depends upon their ability to distort the barium-filled viscera that surround them. Whether it is by pressure due to the mass or actual invasion, it is the distorted barium profile that holds the key to the diagnosis.

*Stomach:* For purposes of detailed description we shall consider the roentgen manifestations anatomically, according to the manner in which the stomach and the

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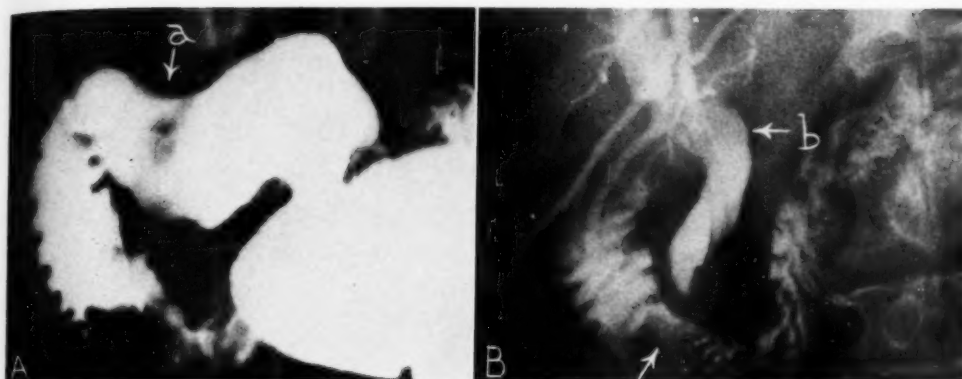


Fig. 2. Carcinoma of the duodenum. Patient 55 years of age complained of jaundice and pain of ten months duration. During this period she had lost 50 lb. in weight. Her stools were clay-colored and her urine dark. At operation the common duct was found to be markedly dilated. There was a walnut-sized tumor involving the posterior wall of the duodenum, due to a primary duodenal carcinoma affecting secondarily the ampulla and common duct. The defect in the distal duodenal loop indicated by the arrow is the duodenal cancer. Note that it is the lateral wall that is primarily invaded. This patient revealed "duodenal impression," *a*, caused by the dilated common duct. The dilated duct, *b*, is revealed by the postoperative cholangiogram, B. By comparing A and B, the "duodenal impression" is clarified.



Fig. 3. Carcinoma of the head of the pancreas. Patient 48 years of age complained of epigastric pain of five weeks duration. He had lost about 8 lb. in weight. His stools were clay-colored and his urine dark. The gallbladder was dilated, and a mass was found in the head of the pancreas invading the common duct. The arrows point to Case's "pad" sign.

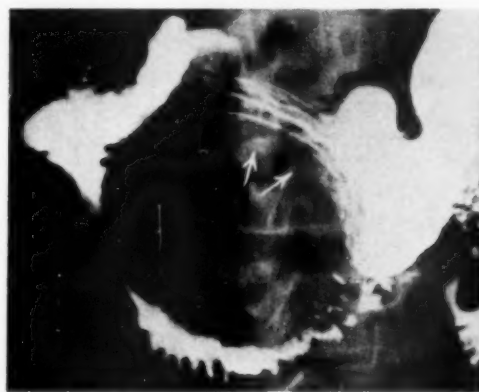


Fig. 4. Carcinoma of the head of the pancreas. A 56-year-old male complained of pain in the epigastrium radiating into the back, of three months duration. During this time he had lost 30 lb. in weight. At operation the common duct was proved to be dilated and a large mass was found in the head of the pancreas due to a carcinoma. The arrows point to the "pad" effect in the antrum. In addition, there is a wide duodenal loop with obvious constriction and invasion in its second and third portions.

various portions of the duodenum are modified.

In tumors arising in the head of the pancreas, the pylorus and antrum are the portions of the stomach that usually are affected. Seen to best advantage in the supine position, these structures may be displaced upward or downward as well as forward.

In his Caldwell lecture in 1939, Case (7)

called attention to the "pad" sign, which he considered highly significant of tumors in the head of the pancreas (Figs. 3 and 4). This he described as a circumscribed filling defect in the gastric silhouette which was seen best in the horizontal position and might disappear completely in the erect position. Due to pressure by the tumor,

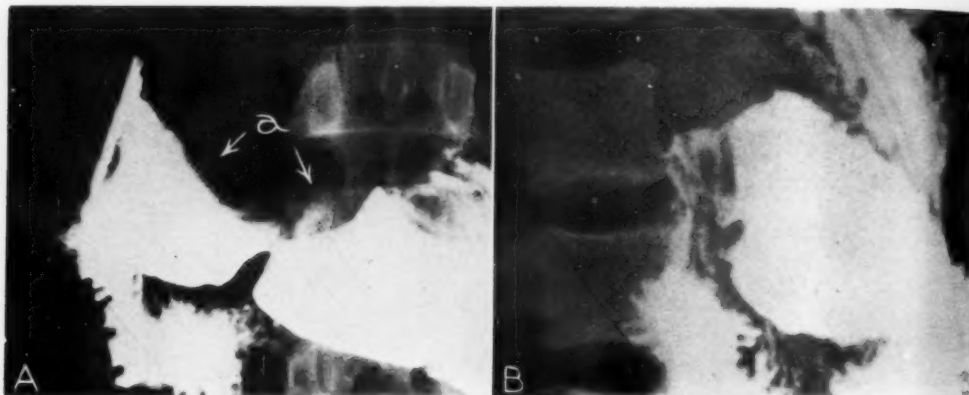


Fig. 5. Carcinoma of the head of the pancreas. Patient 50 years of age complained of jaundice and itching for six months. During this time he had lost 20 lb. in weight. His stools were light and urine dark. At operation, a firm large carcinoma of the head of the pancreas was found which did not affect the common duct or gallbladder. The "pad" defect caused by the tumor is seen at *a*. B is a lateral exposure which reveals no forward displacement of the duodenum or pylorus.

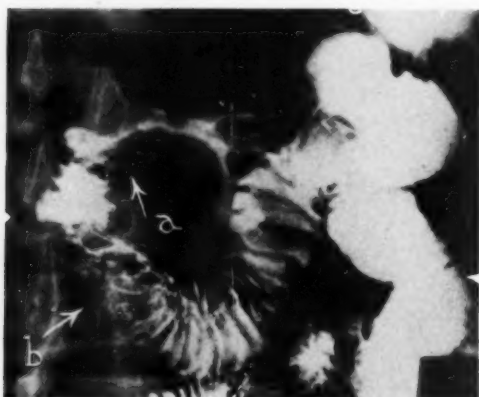


Fig. 6. Carcinoma of the head of the pancreas. Patient 75 years of age complained of jaundice and pruritus and pain of three months duration. His stools were clay-colored and his urine dark. At operation, the gallbladder was seen to be markedly distended and a nodular indurated mass at the head of the pancreas, representing a carcinoma, was found. The duodenum is displaced upward due to the "pad" effect at *a*. Invasion of the duodenum causing mucosal distortion is seen at *b*.

the "pad" effect may be reproduced in the erect position by carefully guided palpation. The effect upon the stomach is not unlike that caused by pressure of the spine, with which it may easily be confused. Confusion may be resolved by examining the patient in the erect position with the abdomen against the fluoroscopic table. If the table is slowly lowered under fluoroscopic control, the "pad" sign due to a

tumor will be recognized long before the table is horizontal enough to cause pressure by the spine upon the barium-filled stomach or duodenum.

Forward displacement of the stomach has been included among the classical roentgen findings in carcinoma of the head of the pancreas. This did not occur regularly in our patients; indeed, in our experience, it was unusual. According to Case there is a tendency in patients with cancer in the head of the pancreas to rapid emptying of the stomach, suggesting achylia. Weigen (37), working with dogs, failed to demonstrate any appreciable change in gastric function in the absence of pancreatic juices. In depancreatized dogs, however, he showed that hyperglycemia seemed to delay gastric emptying while hypoglycemia increased it to a slight degree.

**Duodenal Bulb:** The "pad" effect may be seen in the duodenal bulb as well as in the stomach. The bulb may be pushed up, down, or forward, the degree of displacement depending upon the size and location of the tumor (Figs. 5 and 6). Sometimes it is the lesser curvature that is affected, sometimes the greater.

Occasionally the duodenal bulb is distorted by a dilated common duct. Affecting more commonly the post-bulbar portion



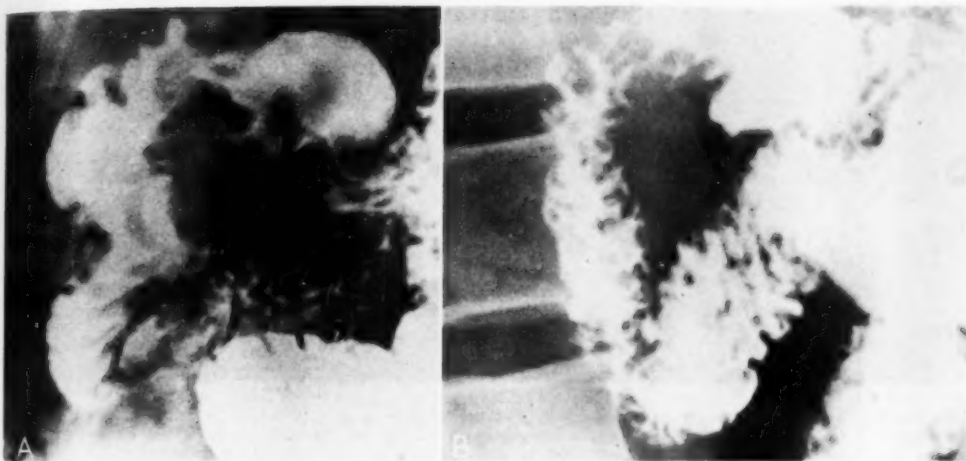


Fig. 7. Carcinoma of the head of the pancreas. The classical inverted "3" is seen in A, with the patient supine. No abnormalities were seen in any other position. The lateral projection in this same patient, B, revealed no abnormalities. Courtesy of Drs. A. Finklestein and D. Zion of Graduate Hospital, University of Pennsylvania.

of the duodenum, this dilated *common duct pressure defect* will be referred to below in fuller detail.

According to some, rapid filling of the duodenal bulb with delayed emptying should suggest disease affecting the duodenal loop. In our experience, arrhythmic and irregular contraction of the duodenal bulb also may be seen.

**Descending Duodenum:** Wide duodenal loops with major duodenal displacement are not the rule. While they do occur, as seen in Figure 4, it is far more common to find the loops normal or but minimally distorted. This leads to errors, for there is a tendency to "over-read" *loop changes* in patients whose clinical history is suggestive of the presence of pancreaticoduodenal disease.

In 1938, Frostberg (15) described the inverted "3" sign, which has received merited acceptance (Fig. 7). Described by Case as "a stopper-like protrusion to the left," the deformity in the descending duodenum may be caused by infection and edema as well as a tumor in the head of the pancreas. As a rule, the inverted "3" is seen best in the supine position. Often it will be seen only in that position, with slight compression, when in all other projections the loop seems normal.

Not infrequently a dilated gallbladder may cause extrinsic pressure upon the duodenal bulb or the descending duodenal limb. The pressure defect usually is a gentle curve with its concavity facing the dilated gallbladder. Much more striking and important are the pressure defects caused by dilated common ducts.

In most individuals the common duct courses behind the duodenum in the immediate post-bulbar region (33). It may lie behind the cap or it may cross the duodenum near the ampulla (Fig. 2). The location of the duodenal defects caused by dilated common ducts depends upon the relationship between the two.

Duodenal pressure defects caused by dilated common ducts are seen best in the prone right anterior oblique or right lateral position (Figs. 8-11). The common duct, lying as it does behind the duodenum, exerts its greatest pressure in these positions. Guided compression in the erect or supine postures also may reveal it (Fig. 12).

The defect suggests extrinsic compression by a pencil-like structure. Usually it looks like an abrupt change in the course of the duodenum. As a rule, it lies in the immediate post-bulbar region, behind which most common ducts lie (Figs. 8-12).

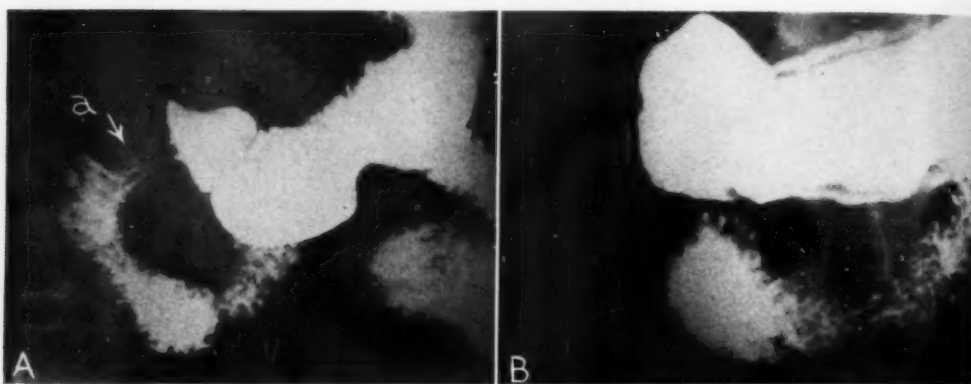


Fig. 8. Carcinoma of the head of the pancreas. Patient 54 years of age complained of generalized abdominal soreness and jaundice of five weeks duration. The stools were light and the urine dark. At operation the gallbladder was distended and the common duct dilated. A large nodular carcinoma of the head of the pancreas was found. The prone right anterior oblique exposure, A, reveals the classical post-bulbar "impression" due to the dilated common duct at *a*. The true prone exposure, B, does not reveal a dilated duodenal loop. Actually the descending duodenal limb may be displaced medially.

Sometimes the cap itself is affected, suggesting duodenal ulcer (Fig. 13).

In 1946 Brown and Harper (4) published a paper entitled "A New Roentgen Sign in Extrahepatic Biliary Tract Disease." In it, they emphasized the importance of duodenal pressure defects caused by dilated common ducts. Though these writers considered this to be a new sign of extrahepatic biliary tract disease, Case (7), Templeton (36), and Feldman (13) had described it previously.

In our opinion, the duodenal defect caused by dilated common ducts (*duodenal impression*) has not received the general recognition or acceptance it merits. Our studies confirm the observations of Brown and Harper. We have watched this sign long enough to consider it a valuable finding in patients with dilated common ducts irrespective of the cause. We are re-emphasizing it now, feeling confident that those who watch for it carefully will, with added experience, come to appreciate its value. It should be emphasized that "duodenal impression" is not pathognomonic for pancreaticoduodenal or ampullary tumors; it will be found in any condition associated with a dilated common duct. It is only fair to state that this sign has its pitfalls.

Occasionally there occurs a normal

change in the course of the duodenum in the immediate post-bulbar area which can be confused with *duodenal impression*. Usually the former is a gentle and gradual change in the configuration of the duodenum, whereas the significant *duodenal impressions* more commonly are abrupt defects sometimes associated with changes in the mucosal pattern. When such confusion exists, the clinical history, physical findings, and cholecystography are valuable. In the presence of a functioning gallbladder, as demonstrated by cholecystography, and absence of clinical findings suggesting common duct or pancreatico-ampullary disease, one should hesitate to attribute significant importance to a questionable *duodenal impression*.

The cystogastrocolic band also may cause confusion. Reported recently by Samuel (31), it may produce changes in the course and configuration of the duodenum that mimic *duodenal impressions*.

Fluoroscopically one often picks up disordered motor function in the descending limb of the duodenum in the presence of these diseases. Normally peristalsis here is even and symmetrical. Most commonly affected is the medial border of the duodenal loop, where limited or even a lack of peristalsis may be observed. The lateral or

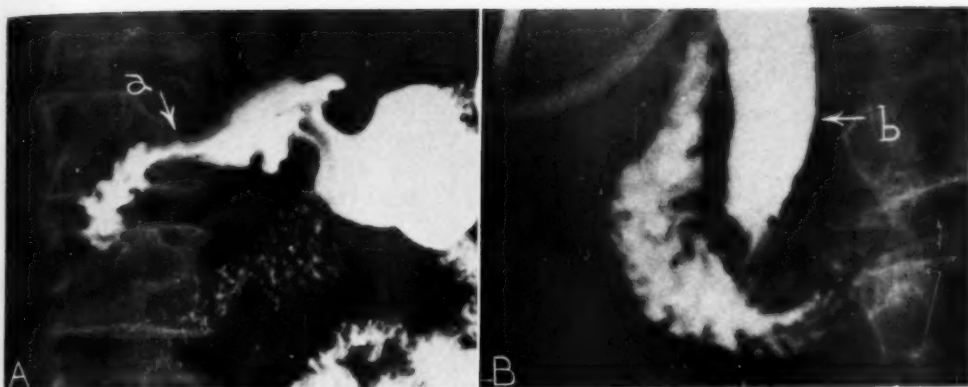


Fig. 9. Carcinoma of the ampulla. Patient 62 years of age complained of pain in the right upper quadrant of three weeks duration. She had lost 20 lb. of weight in eight months. Her stools were clay-colored and the urine dark. A carcinoma of the ampulla of Vater was found at operation. A post-bulbar "impression" is seen at *a* in the exposure made in the prone right anterior oblique position, A. The postoperative cholangiogram, B, reveals the dilated common duct, *b*, with the stenosing lesion infiltrating its ampullary portion.

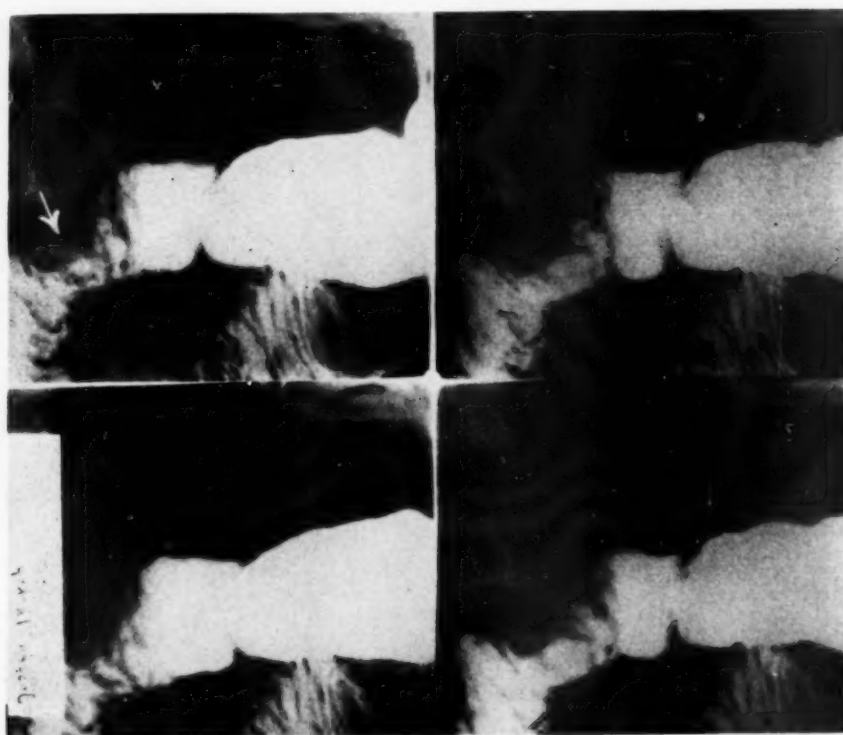


Fig. 10. Carcinoma of the common duct. Patient 48 years of age complained of abdominal discomfort, jaundice, and nausea for four months. His stools were clay-colored and his urine dark. At operation the common duct was greatly dilated. A small lesion at the junction of the pancreatic and common ducts was found, which proved to be a carcinoma. The arrow indicates the post-bulbar "impression" due to the dilated common duct. The examination was made in the prone right anterior oblique position.



Fig. 11 (left). Post-bulbar "impression" at *a*, the result of a dilated common duct due to gallstones. The roentgenogram was made in the lateral position with the patient on the right side.

Fig. 12 (right). Carcinoma of the common duct. Patient 50 years of age with jaundice of three months duration. His stools were clay-colored and his urine dark. At operation, the common duct was markedly distended and a hard mass was found in the duodenal wall invading the common duct, which proved to be a carcinoma of the common duct. This roentgenogram was made in the supine position with the patient in the slight Trendelenburg posture. Note the duodenal defect, *a*, caused by the dilated common duct.

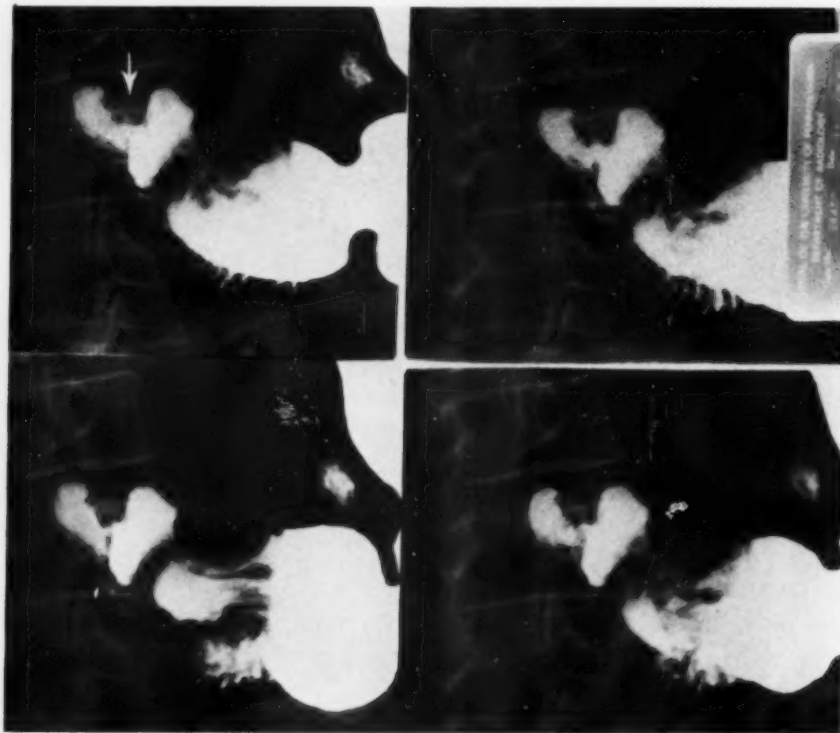


Fig. 13. Carcinoma of the head of the pancreas. Patient 72 years of age complained of pain in the epigastrium, radiating into the right subcostal region and right shoulder, for one year. During this time she had lost 40 lb. in weight. Her stools were clay-colored and urine dark. Cholecystography revealed an abnormal functioning gallbladder. At operation the gallbladder was distended and the common duct dilated as a result of a large carcinoma in the head of the pancreas. The serial roentgenograms reveal a defect in the cap (indicated by the arrow) which was misinterpreted as a duodenal ulcer rather than the "duodenal impression" it actually proved to be. The roentgenograms were made in the prone right anterior oblique position.



Fig. 14. Carcinoma of the head of the pancreas. Patient 40 years of age complained of weight loss and jaundice of several months duration. During this period he had lost approximately 30 lb. in weight. At operation a carcinoma of the head of the pancreas was found. A classical "pad" sign is seen at *a* in the prone exposure, A. The prone right anterior oblique film, B, has recorded the changes observed fluoroscopically in the autoplasty of the duodenal mucosa. The folds are partially obliterated at *b*.

outer border of the loop may not be at all affected until late.

Close fluoroscopic attention to the autoplasty of the duodenal mucosal folds also reveals valuable information. Normally the mucosal pattern changes constantly in uniform and symmetrical manner. The folds are supple, waving or churning freely in the stream of barium, ever influenced by the peristaltic contractions which alter the size of the duodenal lumen and, with it, the mucosal pattern.

All this may change in the presence of disease when the duodenum is infiltrated. Instead of rhythmic and cyclic mucosal fold activity, the autoplasty may be interfered with or entirely lost. Folds may change abruptly in height and thickness. In one area they may look perfectly normal, in another distinctly abnormal. This is particularly true of the mucosa along the medial wall of the duodenal loop.

The importance of excellent roentgeno-

grams for recording permanently these fluoroscopic observations cannot be overemphasized (Fig. 14). Gross changes in advanced tumors can be recognized easily, fluoroscopically. The very early changes—changes that may have been but suspected or even overlooked fluoroscopically—can be demonstrated only in appropriate serial roentgenograms.

The descending duodenal loop may be entirely normal. The early manifestations are slight alterations in the height and width of the mucosal folds along its medial border. Blunt folds may appear anywhere along the barium profile (Fig. 14). Usually they lie proximal to the ampulla. Should diverticula arise in this region, they too may be displaced, a highly significant finding (Fig. 15). Occasionally false diverticula may appear due to necrosis and ulceration of the malignant tumor which communicates with the lumen of the duodenum. These are less regular and more rigid than true





Fig. 15. Carcinoma of the head of the pancreas. Patient 65 years of age complained of epigastric pain of six months duration. He had lost approximately 50 lb. in weight during this period. At operation the gallbladder was found to be dilated and filled with stones. A large mass in the head of the pancreas due to a carcinoma was present. A roentgenogram made in the prone position reveals displacement of a duodenal diverticulum.

diverticula. They commonly cause hemorrhage. With further invasion more obvious changes in the mucosal pattern become manifest, until finally no semblance of normal mucosal folds remains. Partial or even total duodenal obstruction may follow (Fig. 4). Sometimes the medial aspect of the duodenal loop assumes a double contour or profile. Whether this is due to invasion plus pressure by the tumor or some other cause, the medial border of the loop seems reduplicated.

We have observed a peculiar duodenal appearance seen in prone exposures made in the true postero-anterior projection (Fig. 16). Instead of curving, the duodenal loop seems straight and is superimposed on the shadows cast by the duodenal bulb and the pyloric end of the stomach. When we first observed this pattern, we thought it was to be explained by a faulty technic. On subsequent examinations, the technic was not faulty, yet the pattern remained the same. Probably due to the combined effects of medial displacement of the descending duodenal limb and infiltration, it is an appearance which once seen is not forgotten.

With the use of Telepaque (Winthrop-Stearns) has come the promise of new

possibilities in the diagnosis of pancreatico-ampullary disease. Using this substance Shehadi (34) demonstrated a dilated common duct by cholecystography in a patient with cancer in the head of the pancreas in the pre-icteric stage. Wider use of Telepaque may prove Shehadi's



Fig. 16. Carcinoma of the head of the pancreas. Patient 49 years of age complained of pain radiating into the region of the umbilicus, of eight months duration. She had lost 30 lb. in weight. Stools were clay-colored and urine dark. At operation the gallbladder was found to be markedly distended. There was a large, hard, indurated carcinoma of the head of the pancreas. The prone exposure reveals singular lack of detail of the stomach, duodenal bulb, and descending limb of the duodenum.

experience a milestone in the recognition of early lesions obstructing the common duct.

#### DISCUSSION

A study of the literature and our own experience have caused us to re-orient our thinking with respect to neoplasms involving the pancreas and the periampullary region. Instead of seeking wide duodenal loops and inverted figure "3's," we now attempt to demonstrate changes in motor function and altered mucosal pattern of the stomach and the duodenum. Instead of looking for gastric or duodenal displacement, we now try hard to demonstrate the secondary manifestations of a dilated common duct. In this way, we are convinced, pancreatico-ampullary tumors will be recognized earlier and fewer will be overlooked.

For purposes of demonstration, we have

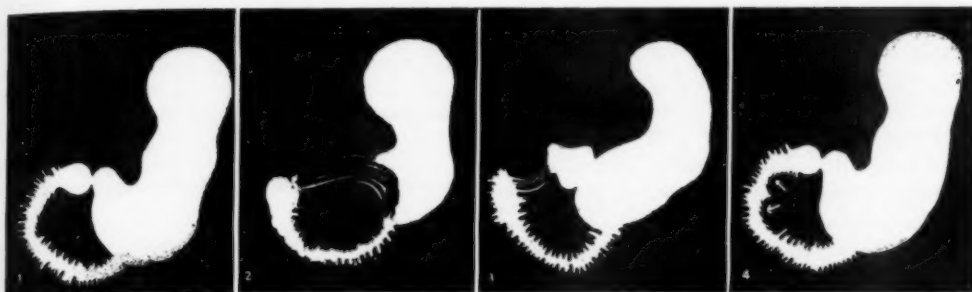


Diagram 1. Early changes in the mucosal pattern of the descending duodenum. The folds here are shorter and thicker. Fluoroscopically they seemed relatively static and did not change pattern and direction with the freedom observed in the neighboring folds.

Diagram 2. Case's "pad" sign. Due to extrinsic pressure by the tumor, it is seen best in the horizontal position.

Diagram 3. Post-bulbar "duodenal impression" caused by a dilated common duct. It is usually seen best in the prone position with the patient in the right anterior oblique posture.

Diagram 4. Frostberg's inverted "3" sign. As a rule the inverted "3" is seen best in the horizontal position with the patient supine. Slight compression may reveal it to better advantage. Note the altered mucosal pattern indicated by the arrows on either side of the teat-like protrusion.

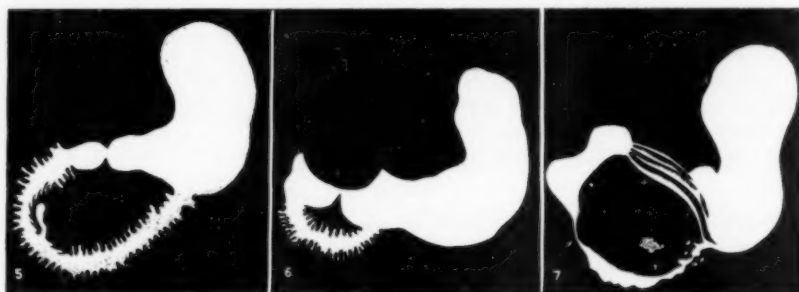


Diagram 5. Diverticulum springing from the descending limb of the duodenum where it is displaced upward. The duodenal loop is a little "full."

Diagram 6. Extrinsic pressure defect caused by a mass in the head of the pancreas at x. The duodenum and stomach are being pushed downward by the mass, but they might just as well have been pushed upward.

Diagram 7. The combined effects of "mass" and "invasion" are here demonstrated. Case's "pad" sign is seen at x. The arrows point to the infiltrated duodenum, which is partially obstructed as well as displaced.

reproduced diagrammatically some of the roentgenograms already included in this text. It is hoped that these will re-emphasize what has been said above. In each instance reference is made in the legend to the original roentgenogram from which the artist reproduced his drawing. No attempt was made to obtain the exact likeness; instead, in each instance we have tried to emphasize fundamental radiological changes.

The earliest changes are seen in Diagram 1 taken from Figure 14. It reveals an altered mucosal pattern only. Case's "pad" sign is easily recognized in Diagram

2, taken from Figure 3. The "duodenal impression" in the post-bulbar region is obvious in Diagram 3, taken from Figure 8. Frostberg's inverted "3" is seen in Diagram 4, taken from Figure 7. In it attention is called to the minor mucosal changes adjacent to the stopper-like deformity. In Diagram 5, taken from Figure 15, the displaced duodenal diverticulum has been recorded. The pressure defect caused by the mass in the duodenum and stomach is depicted in Diagram 6, taken from Figure 5. For obvious reasons this defect might just as well have affected the greater curvature side of the antrum of

the stomach and the duodenal bulb. We chose this one because it was less common. Diagram 7, taken from Figure 4, merely combines the effects of a large mass which not only has produced a "pad" sign but also has infiltrated and partially occluded the duodenal loop, which has lost all semblance of its normal mucosal pattern.

Lest these diagrams be misinterpreted, we hasten to state that these are not the only roentgen abnormalities produced by the tumors of the pancreas and periampullary region. Nor should they be looked upon as pathognomonic. What we have tried to do is stress cardinal roentgen findings, findings which too often have been ignored.

#### CONCLUSIONS

1. It is often difficult or impossible to differentiate pathologically between various tumors that arise in the pancreatico-ampullary region. For this reason they often cannot be told apart roentgenologically.

2. The clinical history in these patients is highly significant and of paramount importance. Pain, jaundice, and loss of weight are cardinal complaints.

3. Pancreatico-ampullary lesions do not commonly produce wide duodenal loops nor do they as a rule displace the duodenum or stomach anteriorly.

4. The majority of cancers in this region cause roentgen changes in duodenal motor activity and duodenal mucosal pattern. Once this is appreciated, the recognition of these tumors should become less difficult.

5. Dilated common ducts often produce *duodenal impressions* in the immediate post-bulbar region or in the bulb itself, which may prove extremely valuable in the recognition of pancreatico-ampullary tumors.

NOTE: We acknowledge with gratitude the assistance given us by Dr. Arthur Finkelstein and Dr. David Zion of the Department of Radiology, Graduate Hospital, University of Pennsylvania, and of Dr. W. Edward Chamberlain of the Department of Radiology, Temple University Hospital. Al-

ways willing to share their experiences with others, these radiologists made available to us many gastrointestinal examinations of patients with proved cancer in the region of the head of the pancreas. Their selfless assistance made it possible for us to augment our own experience, thereby allowing us to express opinions based upon many more patients than those studied in our own department.

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## SUMARIO

## Neoplasias del Páncreas, del Colédoco y de la Papila de Santorini: Sus Manifestaciones Roentgenológicas

Propónense los AA. sumarizar las manifestaciones roentgenológicas de las lesiones carcinomatosas de la cabeza del páncreas, de la papila o ampolla de Santorini (o Vater) y del colédoco, recalcando de nuevo y enfocando las observaciones ajenas a la luz de las propias.

Resulta a menudo difícil, sino imposible, diferenciar histopatológicamente esos diversos tumores de la región pancreato-papilar, y con frecuencia no pueden distinguirse entre sí roentgenológicamente.

La historia clínica reviste importancia primordial, siendo los principales sínto-

mas dolor, ictericia y pérdida de peso. Los hallazgos radiológicos son semejantes para todos los tumores pancreato-papilares. Los que hay que considerar mayormente no son la dilatación del asa duodenal o el desplazamiento gástrico o duodenal sino más bien las alteraciones de la actividad motora del duodeno y del patrón de la mucosa de este órgano. Un signo que puede resultar sumamente valioso es la llamada impresión duodenal producida en la inmediata región postbulbar o, a veces, en el capuchón mismo, por un colédoco dilatado.

# Roentgenologic Observations in Addison's Disease

## A Review of 120 Cases<sup>1</sup>

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DURING RECENT years remarkable progress has been achieved in the diagnosis and treatment of adrenal insufficiency. The availability of potent and highly purified preparations of the adrenocorticotrophic hormone (ACTH) has resulted in the development of improved diagnostic procedures for the evaluation of adrenocortical function. The isolation, synthesis and large scale production of individual adrenal cortical steroids which are highly effective in replacement therapy have greatly altered the prognosis of a disease once considered almost hopeless. As a consequence of these advances, an ever increasing number of patients with chronic adrenal cortical insufficiency are being successfully maintained in an active and productive state. In the overall clinical management of these patients, roentgen examination may play an important role. It is the purpose of this report to summarize the results of roentgenologic observations made during the past twenty years in patients with Addison's disease observed at the Peter Bent Brigham Hospital.

### METHODS

This study is based on the roentgenologic examinations of 120 patients. The following criteria have been employed for inclusion in this series: (a) *History*: Although the symptoms of Addison's disease are often non-specific, certain manifesta-

tions are almost constantly present: fatigability, muscular weakness, weight loss, anorexia, and gastrointestinal symptoms.

(b) *Physical Examination*: Hypotension is an almost invariable finding in untreated patients. Characteristic pigmentation of the skin and mucous membranes is found with such great regularity that its absence casts considerable doubt upon the diagnosis.

(c) *Laboratory Findings*: Hyponatremia, hyperkalemia and azotemia are commonly encountered in untreated patients, especially those in whom the disease is of long duration or in whom adrenal crisis may be imminent. It is to be emphasized, however, that in many instances these values are normal. Electroencephalographic changes are highly suggestive of Addison's disease, although an abnormally slow pattern may be encountered in situations other than adrenal insufficiency (e.g., myxedema).

(d) *Special Tests*: All patients admitted since 1947 have undergone vigorous testing with adrenocorticotrophic hormone, (ACTH). In normal subjects, stimulation of the adrenal cortex by ACTH produces numerous metabolic and cytologic changes, of which a fall in circulating eosinophils and a rise in urinary steroid excretion serve as convenient and accurate indices of adrenal cortical activation (1). Since patients with Addison's disease fail to exhibit these characteristic responses, the

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ACTH test provides a highly specific and reliable means of establishing or confirming the diagnosis of adrenal insufficiency. Other indices which have been employed in the diagnostic study of these patients include a significant delay in diuresis following an acute water load (Robinson-Power-Kepler); an incapacity to conserve body sodium and chloride under conditions of salt restriction (Cutler-Power-Wilder); a marked susceptibility to hypoglycemia produced by insulin administration or prolonged fasting.

The patients studied (Table I) included

TABLE I: ONE HUNDRED AND TWENTY CASES OF ADDISON'S DISEASE

Age*	Males	Females	Totals
10-19	2	3	5
20-29	7	6	13
30-39	17	13	30
40-49	10	20	30
50-59	14	17	31
60-69	5	5	10
70-	1	0	1
TOTALS	56	64	120

\* At time of last x-ray examination.

64 females and 56 males, ranging in age from ten to seventy-one years, the majority (80 per cent) being between twenty-five and fifty years of age. Eighty-six patients are living and are currently under treatment; 31 patients are dead; the present status of 3 patients can not be ascertained. Postmortem examinations have been obtained in 17 cases, including 12 performed at this institution, and the findings have been correlated with those of the present study. Adequate roentgenologic examinations were carried out in these patients within one year of death.

Of the 86 patients now living, 63 have been examined in both the department of radiology and the medical clinic within the past year. The therapeutic management of this group has been recently described (2).

Roentgenologic examination of the chest, skull, and abdomen has been performed in the majority of patients. All films were initially interpreted by one of the authors (M.C.S.). Subsequently, all available

TABLE II: ADRENAL CALCIFICATION IN 106 PATIENTS WITH ADDISON'S DISEASE

	Bilateral	Right	Left	Totals
Males	10	2	3	15
Females	3	1	5	9
TOTALS	13	3	8	24

films have been thoroughly reviewed and the findings correlated with clinical data. Films taken at other hospitals have been examined when available.

#### OBSERVATIONS

**Adrenal Calcification:** X-ray evidence of adrenal gland calcification in Addison's disease was originally reported by Rolleston and Boyd (3) in 1914, the patient having been examined roentgenologically by Melville. Numerous reports of individual cases in which adrenal calcification has been visualized have since appeared (4-9). In 1932, Ball *et al.* (10, 11) reported on the detailed radiologic examination of a series of patients with unmistakable evidences of Addison's disease. Calcified areas in the region of the adrenal glands were discernible in 6 of 23 patients examined during life. In 11 of 34 cases examined postmortem, x-rays of the removed adrenal glands revealed easily visible calcification, of which three types were described: (a) gross calcification of the gland; (b) multiple discrete deposits of calcium, and (c) homogeneous increase in density of the entire gland shadow.

In the present study, the adrenal regions were studied by means of anteroposterior films of the abdomen. Tomograms were obtained in a number of patients in an attempt to improve visualization of calcified areas or to demonstrate calcific deposits not visible on routine examination. No adrenal calcification was demonstrated by this procedure which had not previously been identified on the survey film of the abdomen.

Satisfactory films of the adrenal regions were obtained in 106 patients. Adrenal calcification was visualized in 24 cases (23 per cent) (Table II). The presence of calcification was verified during nephrec-

tomy in 2 patients, and in 2 others at postmortem examination. In 2 patients the initial evidence of calcification developed during a ten-year period of observation, and 1 additional case showed a definite increase in the amount of calcium during a similar period. The calcified adrenal gland is usually demonstrable as a triangular or irregular shadow located over the medial aspect of the upper pole of the kidney (Fig. 1), and ordinarily appears to be composed of numerous small, dense discrete concretions. No instance of total, or homogeneous calcification of the gland was observed in our series of patients.

During the period covered by this report, 4 additional patients with calcification in the suprarenal area have been encountered in whom adrenal cortical function was demonstrated, by the diagnostic criteria cited above, to be intact. The appearance of these calcific areas, unilateral in 1 instance and bilateral in 3, was indistinguishable roentgenologically from that in patients with proved adrenal cortical insufficiency. The following case is representative:

A. A., a 30-year-old female, entered the Peter Bent Brigham Hospital with a presumptive diagnosis of Addison's disease. Nine years prior to admission, she had complained of fatigability and noted moderate but persistent pain in the lumbar area, bilaterally. X-ray examination of the lumbar spine at that time revealed bilateral adrenal calcification, and a diagnosis of Addison's disease was entertained. Intensive study at another hospital, however, failed to substantiate the diagnosis. Nine weeks before the present admission, pain again occurred in the lumbar area, with radiation to the left hip.

Physical examination revealed a well nourished female in whom no abnormal pigmentation could be detected and whose blood pressure was 126/78 mm. Hg. Routine laboratory studies were normal. The Robinson-Power-Kepler water test, a salt-deprivation test (Cutler-Power-Wilder), and an intravenous glucose tolerance test were all normal. The adrenal cortical response to ACTH was entirely normal. Roentgen examination of the lungs was negative. Films of the abdomen revealed large, finely granular areas of calcification in each adrenal area (Fig. 2).

In spite of the lack of definitive evidence to support a diagnosis of adrenal insufficiency, the patient was given a fourteen-day trial of desoxycorti-

costerone acetate, 2.5 mg. per day. The treatment resulted in no symptomatic improvement. Follow-up studies during the past six years have confirmed the presence of intact adrenal cortical function. It is therefore concluded that, in spite of bilateral adrenal calcification, this patient at present has normal adrenal cortical function.

It is evident, therefore, that suprarenal calcification is *not* pathognomonic of adrenal cortical insufficiency. The discrepancy can, in all likelihood, be explained by the findings of Barker (12), who demonstrated in a detailed autopsy study of 28 cases of Addison's disease that the clinical manifestations of adrenal insufficiency became apparent only when 90 per cent or more of the adrenal cortical tissue had been destroyed. It is equally evident, however, that the presence of adrenal calcification constitutes presumptive evidence for the disease and indicates the need for thorough diagnostic study.

In view of the recognized importance of tuberculosis in the pathogenesis of Addison's disease, an attempt has been made to correlate the existence of adrenal calcification with the actual presence of the former disease. Of the 24 patients in the authors' series with adrenal calcification, 11 (46 per cent) showed no evidence of pulmonary tuberculosis, 6 (25 per cent) presented the typical findings of old inactive tuberculosis, and 7 (29 per cent) exhibited unequivocal evidence of active pulmonary tuberculosis. The latter group is considered to be particularly important since, of the 9 cases in the entire series with clinically demonstrable *active* tuberculosis, 7 revealed adrenal calcification.

*Heart Size:* Addison's disease is characterized by important abnormalities of cardiovascular function, including hypotension, a low pulse pressure, a diminished blood volume, and a small heart. The latter, which is most accurately and conveniently determined by teleroentgenography (13), constitutes a useful guide in the regulation of substitution therapy. *In the authors' experience, no patient with untreated and uncomplicated Addison's disease has been encountered in whom cardiac*



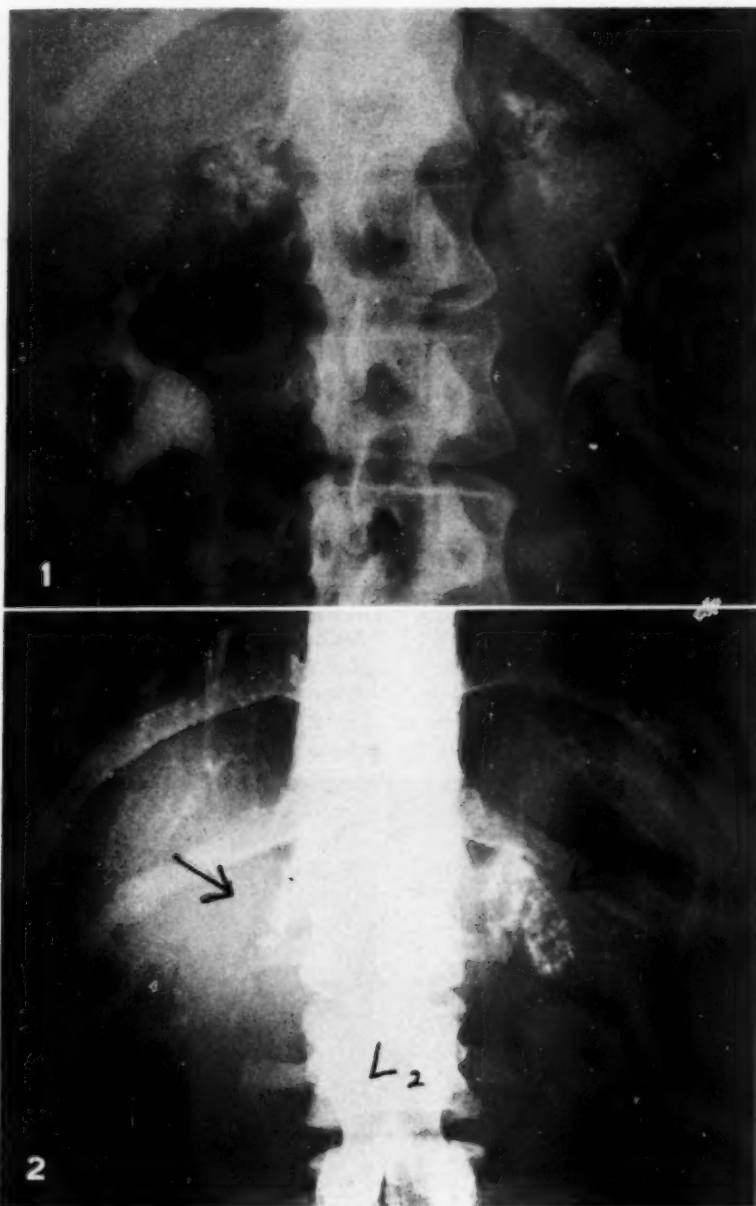


Fig. 1. Bilateral adrenal calcification in a patient with Addison's disease.

Fig. 2. Bilateral adrenal calcification in a patient with intact adrenal cortical function. The calcification is more extensive on the left side, which may indicate that the right adrenal is only partly involved.

*enlargement was demonstrable.* The institution of specific therapy is characteristically followed by an elevation of blood pressure and increased cardiac output, a rise in blood volume, and a return of the cardiac

dimensions toward normal. In evaluating maintenance treatment with desoxycorticosterone, the hormone chiefly responsible for the retention of sodium, chloride, and water (and therefore for the restitution of

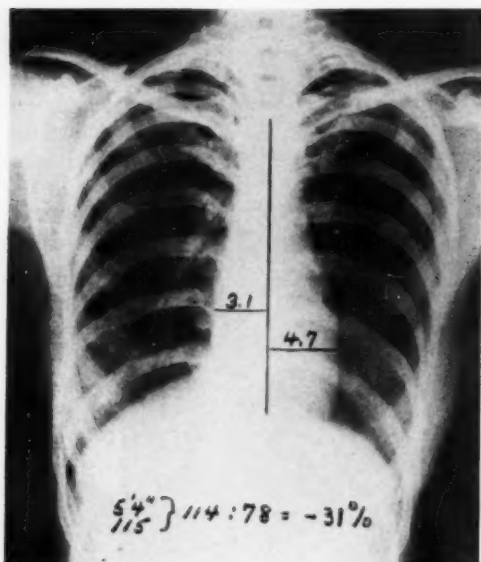


Fig. 3. Marked reduction in cardiac dimensions in an untreated patient with Addison's disease. Figures denote: height, weight (pounds), predicted cardiac transverse diameter (mm.), measured cardiac transverse diameter (mm.).

blood volume), the resultant alteration in heart size may be an extremely valuable

adjunct to clinical judgment and to other laboratory measurements. The administration of excessive quantities of desoxycorticosterone is usually accompanied by a rapid gain in weight, the appearance of peripheral edema, and frequently hypertension. In conjunction with these changes, cardiac size as determined by roentgen examination may increase well above the limits of normal.

In this study, the transverse diameter of the heart, measured on a 7-foot film of the chest taken during average inspiration was compared with the normal or predicted cardiac diameter calculated on the basis of body height and weight according to the method of Ungerleider and Clark (14). This measurement was obtained initially on all patients and followed serially thereafter during the entire period of study. In fact, such a heart film is routinely obtained in the follow-up studies of all patients with Addison's disease in this clinic. Some patients included in this group have now undergone more than fifty examinations during the past fifteen years. In evaluating the accumulated data, all available films

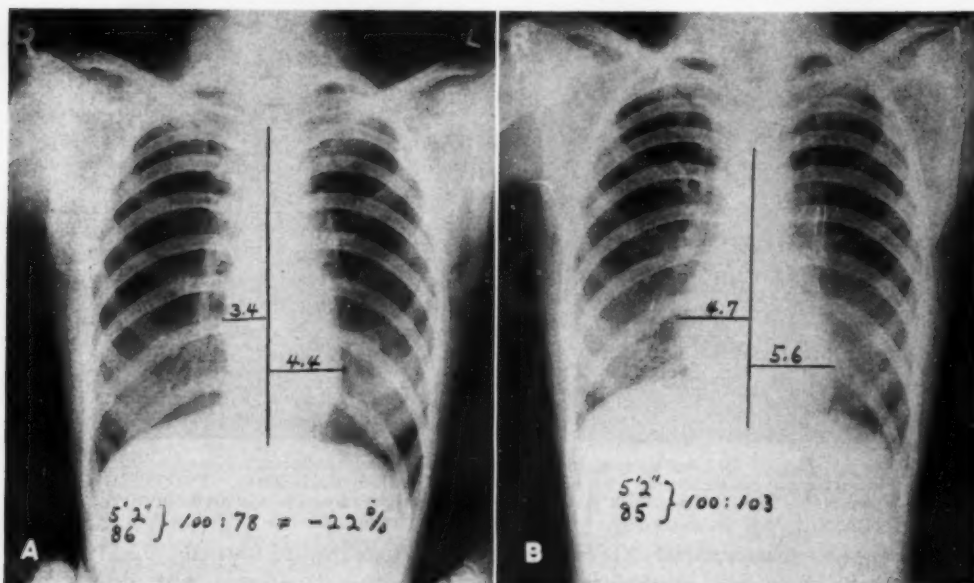


Fig. 4. Effect of treatment with desoxycorticosterone acetate on heart size in Addison's disease.

A. Significant reduction in heart size in a patient with Addison's disease prior to hormone treatment.

B. Restoration of heart size to normal, in the same patient, following treatment with desoxycorticosterone acetate for fourteen days.

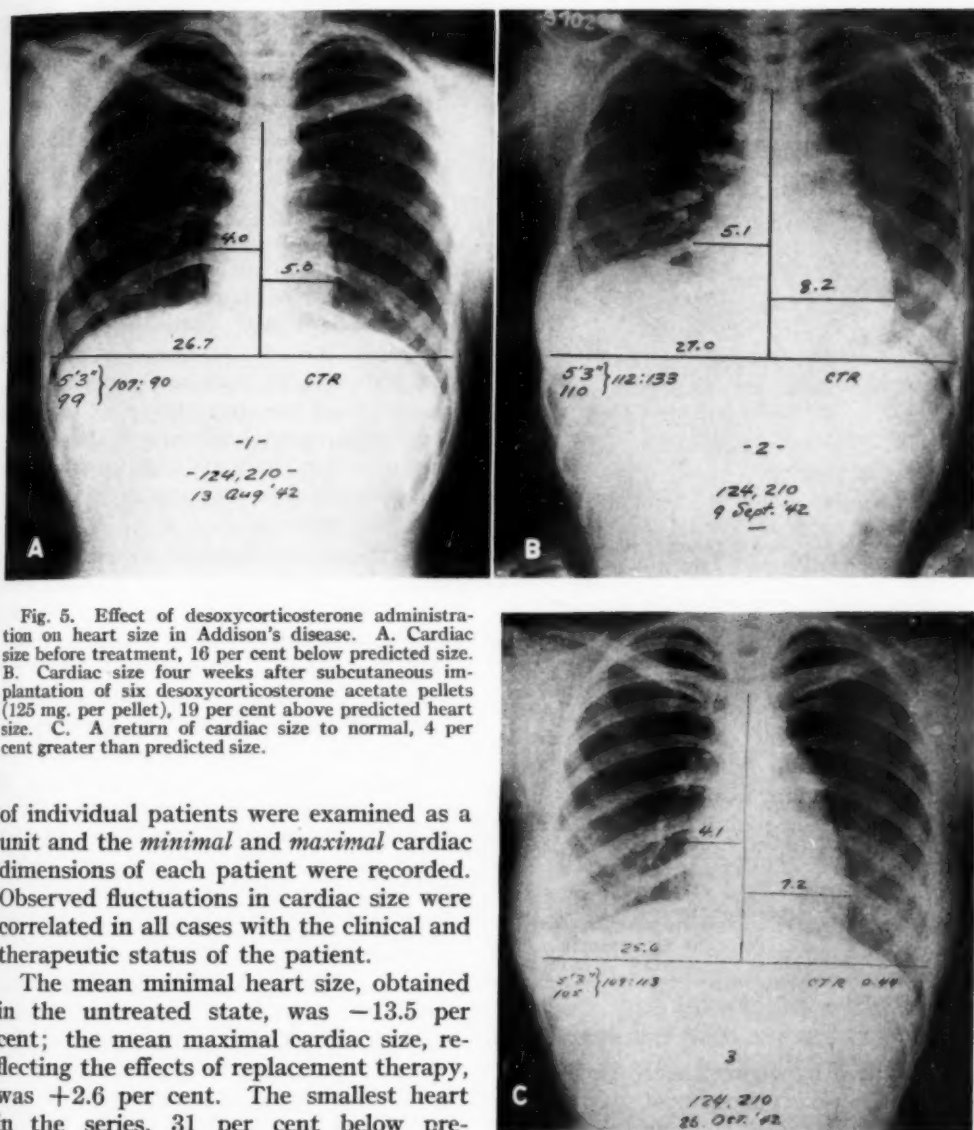


Fig. 5. Effect of desoxycorticosterone administration on heart size in Addison's disease. A. Cardiac size before treatment, 16 per cent below predicted size. B. Cardiac size four weeks after subcutaneous implantation of six desoxycorticosterone acetate pellets (125 mg. per pellet), 19 per cent above predicted heart size. C. A return of cardiac size to normal, 4 per cent greater than predicted size.

of individual patients were examined as a unit and the *minimal* and *maximal* cardiac dimensions of each patient were recorded. Observed fluctuations in cardiac size were correlated in all cases with the clinical and therapeutic status of the patient.

The mean minimal heart size, obtained in the untreated state, was  $-13.5$  per cent; the mean maximal cardiac size, reflecting the effects of replacement therapy, was  $+2.6$  per cent. The smallest heart in the series, 31 per cent below predicted size, was encountered in a 44-year-old female first seen eighteen months after the cessation of replacement therapy (Fig. 3). Figure 4 shows (A) the characteristically small heart of an untreated patient, bordering upon adrenal crisis at the time of examination, and (B) the subsequent reversion to normal size following the institution of adequate hormone therapy. For comparison, Figure 5 shows the results of moderate desoxycorticoster-

one acetate overdosage with a resultant increase in heart size from (A)  $-16$  per cent prior to the subcutaneous implantation of six desoxycorticosterone pellets, to (B)  $+19$  per cent four weeks following implantation, with (C) a subsequent return to normal following the removal of two desoxycorticosterone pellets.

In patients with normal heart size, considerable caution is advisable in the admin-

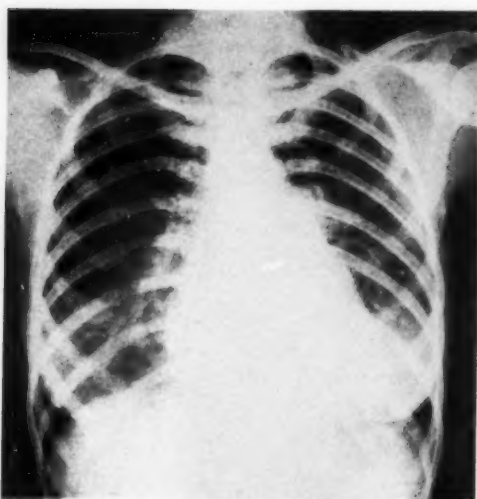


Fig. 6. A twenty-five-year-old female with Addison's Disease of ten years duration. Rheumatic heart disease with mitral stenosis diagnosed two years prior to this examination. Predicted transverse cardiac diameter, 109 mm.; measured transverse cardiac diameter, 142 mm. (+33 per cent). Because of progressive signs of congestive failure, this patient recently underwent a successful mitral valvuloplasty.

istration of desoxycorticosterone. In the presence of a heart of *normal* size in an untreated patient with Addison's disease underlying organic heart disease (Fig. 6) or hyperthyroidism should be suspected. On the other hand, in adrenal insufficiency

TABLE III: HEART SIZE IN 120 PATIENTS WITH ADDISON'S DISEASE

	Per Cent Males	Predicted Size Females	Average
Mean minimal	-12	-15	-13.5
Mean maximal	+3	+2.5	+2.8

complicated by organic heart disease, evidence of cardiac enlargement may be minimized by dehydration, hypotension, and a decrease in blood volume. The initiation of specific hormone therapy, especially desoxycorticosterone, is usually followed in these patients by the prompt appearance of cardiac enlargement above normal and, in some cases, by the appearance of characteristic heart murmurs. The proper regulation of hormone therapy may thus be considerably more difficult than in uncomplicated Addison's disease. Indeed, these patients may be able to tolerate only the

TABLE IV: PULMONARY FINDINGS IN 116 CASES OF ADDISON'S DISEASE

I. Normal	60
II. Inactive tuberculosis	
Ghon complex	7
Pleural thickening	5
Inactive parenchymal lesion	23
Diffuse parenchymal calcification	1
Thoracoplasty	2
III. Active tuberculosis	38
Moderately advanced	6
Far advanced	3
	9

smallest doses of desoxycorticosterone so that treatment with cortisone only, and supplementary salt as required to maintain ideal body weight, may be the most efficacious form of therapy. In order to effect the best therapeutic response in these combined disorders, frequent determinations of heart size by teleroentgenogram may prove extremely valuable.

It is apparent that serial examinations of cardiac size with a carefully standardized technic provide a quick and convenient guide to the maintenance of optimal substitution therapy in patients with Addison's disease. Treatment with desoxycorticosterone ordinarily should not be initiated without a preliminary determination of heart size. During the early stages of therapy, periodic heart measurements may aid materially in determining optimal maintenance hormone dosage. A reduction in desoxycorticosterone dosage is ordinarily indicated when heart size approaches normal.

**Lungs:** The results of roentgen examination of the chest in 117 patients are summarized in Table IV. It is apparent that 69 patients (59 per cent) presented no detectable evidence of pulmonary disease. In 39 patients (33 per cent), the findings were considered to be consistent with inactive pulmonary tuberculosis. Active tuberculous disease could be demonstrated in only 9 cases (8 per cent). Of the latter, 6 have been classified as moderately advanced and 3 as far advanced, on the basis of the criteria of the National Tuberculosis Association (15).

These data are of interest in relation to present concepts concerning the etiology and pathogenesis of Addison's disease.

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Two pathological conditions are mainly responsible for bilateral adrenal cortical destruction: fibrocaceous tuberculosis and an idiopathic process resulting in adrenal cortical necrosis and atrophy. Older reports emphasized the preponderance of tuberculosis as the etiologic agent. For example, in a review of 566 cases of Addison's disease with postmortem studies, Guttman (16) in 1930 described bilateral adrenal tuberculosis as the etiologic factor in 70 per cent. It is of interest, therefore, that 59 per cent of the patients in this series revealed no radiologic evidence of either active or healed pulmonary tuberculosis. Furthermore, the low incidence of active pulmonary lesions (8 per cent) emphasizes the fact that Addison's disease, even when due to adrenal tuberculosis, is not commonly associated with active disease in the lungs. Since the primary lesion, in the vast majority of tuberculous infections, is situated in the lung, it would appear that adrenal insufficiency does not materially impair the mechanisms of natural and acquired resistance which ultimately must determine the course of tuberculosis. Indeed, it is the authors' clinical impression that patients with adrenal insufficiency are, in general, suprisingly resistant to tuberculous infections and usually succeed in effectively localizing the disease.<sup>6</sup>

It is of interest that among the 12 autopsies performed in this institution, 6 cases showed adrenal tuberculosis and 6 revealed idiopathic atrophy. Although the number of autopsies is too small to warrant statistical generalization, the incidence both of pulmonary tuberculosis as determined by roentgen examination and adrenal tuberculosis found postmortem is in agreement with the opinion (17) that the pro-

portion of cases of Addison's disease due to tuberculosis is decreasing.

*Spleen:* Films of the abdomen affording a suitable evaluation of spleen size were obtained in 106 cases. Definite splenomegaly was evident in 10 patients (9 per cent), 7 males and 3 females. In no instance, however, was the spleen sufficiently enlarged to be palpable on physical examination. Of this group, only 1 patient presented evidence of active pulmonary tuberculosis. Of the 12 patients examined postmortem in this institution, 10 exhibited slight to moderate splenomegaly, with spleen weights ranging from 190 to 350 gm. In the latter group there were 3 cases of active tuberculosis, 3 of inactive, well healed tuberculosis, and 4 in which no signs of the disease could be found. Rowntree and Snell (18) also noted a moderate degree of splenomegaly in 8 of 31 cases of Addison's disease examined postmortem. The enlargement in most cases was slight and not considered by the authors to be significant.

Since no significant correlation between the existence of splenomegaly and the presence of active tuberculous disease is apparent, it is not unlikely that the splenomegaly, discernible by roentgen examination but not ordinarily detectable on physical examination, may well reflect the generalized hyperplasia of the lymphatic system commonly seen in patients with Addison's disease. In keeping with this hypothesis, 5 of the 10 patients revealed either a normal or definitely reduced spleen size following the institution of cortisone therapy.

In view of the fact that lymphatic tissue throughout the body is ordinarily increased in amount in patients with untreated Addison's disease, demonstration of thymus enlargement by roentgenologic means might well be anticipated. To date, however, no enlargement or tumor of the thymus has been recognized.

*Gastrointestinal Tract:* Examination of the upper gastrointestinal tract was carried out in 24 patients. Twenty of these studies were entirely negative. Two pa-

<sup>6</sup> In contrast to the increased resistance of Addisonian patients to tuberculosis, it is now well known that prolonged administration of ACTH or cortisone to patients with intact adrenal cortices may have a deleterious effect on pulmonary tuberculosis. The authors' series of Addisonian patients with active tuberculosis who are receiving maintenance doses of cortisone (12.5-25 mg. per day) is too small to permit conclusions as to whether such therapy may aggravate the tuberculous lesions. No such aggravation, however, has been observed to date.

tients showed a deformity of the duodenal bulb without a demonstrable crater, considered to be characteristic of healed peptic ulcer. One of these patients is presently maintained on 60 mg. of long-acting desoxycorticosterone trimethylacetate administered intramuscularly at thirty-day intervals, and 25 mg. of cortisone acetate by mouth daily. There are no symptoms referable to the lesion described, and neither alkali ingestion nor strict dietary control is necessary. The other patient, however, is unable to take the usual maintenance doses of cortisone because of the occurrence of post-prandial epigastric pain. Maintenance therapy, therefore, consists of 60 mg. of desoxycorticosterone trimethylacetate at monthly intervals plus a moderately strict ulcer diet.

Two patients presented interesting and somewhat unusual findings:

E. M., a 47-year-old female, entered the hospital in 1949 in adrenal crisis precipitated by an acute episode of severe gastroenteritis. Following emergency therapy with desoxycorticosterone, adrenal cortical extract, and intravenous fluids, the patient was discovered to have melena. Roentgen examination at this time revealed a shallow lesion on the lesser curvature of the stomach having the appearance of a benign gastric ulcer. Gastroscopy, however, showed a hemorrhagic erosive gastritis, and the gastroenterologist did not consider the lesions to be those of peptic ulcer. This patient had not previously received cortisone. After re-establishment of maintenance hormonal therapy, subsequent roentgen examination of the upper gastrointestinal tract revealed complete healing of the gastric lesion. The patient is currently maintained on 12.5 mg. of acetate every thirty days, without the recurrence of melena or symptoms of an active gastric lesion.

While it is now well known that episodes of the above type may occur in the presence of excessive circulating adrenal cortical hormone, *e.g.*, during the administration of ACTH or cortisone to patients with intact adrenal cortices, it is less well appreciated that gastrointestinal lesions of this type may be observed in association with adrenal cortical insufficiency. Such lesions have been found in patients who have died in Addisonian crisis. Moreover, animals dying of acute adrenal insufficiency com-

monly exhibit marked hyperemia of the gastrointestinal tract, frequently accompanied by widespread ulceration of the gastric mucosa (19). On the other hand, gastric ulceration has been described in human beings as well as animals subjected to overwhelming stress, *e.g.*, severe burns. It has been postulated that lesions of the latter type develop in association with a relative deficiency of adrenal cortical hormones, since adrenalectomy significantly increases the susceptibility of the organism to their occurrence (20). It is therefore possible that the superficial hemorrhagic and ulcerative gastric lesions which may occur during adrenal crisis are a consequence of changes, not yet understood, induced by severe stress and facilitated by an absolute or relative deficiency of adrenal cortical steroid hormones. Lesions of this type ordinarily heal promptly following adequate hormone replacement therapy and recovery from adrenal crisis.

A. T., a 61-year-old male with Addison's disease of sixteen years duration, was admitted to the hospital because of persistent melena. From 1939 until 1950 the disease was adequately controlled by the periodic subcutaneous implantation of desoxycorticosterone acetate pellets. During the past three years the patient had also received 12.5 mg. of cortisone acetate daily by mouth. Two months prior to his most recent hospital admission epigastric distress had developed, accompanied by melena. Two roentgenologic examinations revealed a typical small peptic ulcer on the lesser curvature of the stomach, which did not appear to be malignant. Gastroscopy confirmed the presence of a gastric ulcer. The patient was placed on a strict ulcer regimen and discharged on desoxycorticosterone trimethylacetate and a reduced dosage of oral cortisone acetate (6.25 mg. per day). Re-examination by both fluoroscopy and gastroscopy three weeks later failed to reveal any evidence of the previously observed lesion. At the present time the patient remains asymptomatic but continues to follow a modified ulcer program.

The frequency of gastrointestinal symptoms in untreated patients with Addison's disease has received due emphasis as a conspicuous element of the clinical syndrome. Moreover, the relationship of the adrenal cortex to gastrointestinal function is complex. On the basis of recent studies, it is

apparent that adrenal cortical hormones, including both desoxycorticosterone and compounds of the cortisone and hydrocortisone type, may exert an important influence on the functions of the entire gastrointestinal system. The following actions may be listed: (a) The electrolyte concentration of saliva, conveniently expressed as a sodium-potassium ratio, is subject to the influence of adrenal cortical steroids (21). (b) Hypoacidity and even anacidity have been described in a high proportion of patients with Addison's disease (18). (c) Detailed studies of gastric secretory function in many of the patients in this series have consistently demonstrated a marked reduction in the urinary excretion of uropepsin (22). Since the output of uropepsin appears to be well correlated with the gastric secretion of peptic enzymes, it is apparent that the presence of adrenal cortical steroid hormones is important for normal secretory and enzymatic function of the stomach. (d) Preliminary studies in this laboratory suggest that cortisone and related steroids are capable of influencing biliary secretion (23). (e) The actions of desoxycorticosterone in reducing sodium excretion and increasing potassium output have been demonstrated to extend to the large bowel (24). It is obvious, therefore, that the integrity of gastrointestinal function depends in part upon a normal level of adrenal cortical function.

As described above, gastritis and superficial gastrointestinal ulceration may be encountered during acute adrenal insufficiency. However, true peptic ulcer in untreated patients with Addison's disease is, in the authors' experience, a rare complication. That this might well be anticipated is evident from the tendency of these patients to have a reduced gastric secretion of both acid and peptic enzymes. On the other hand, the high degree of sensitivity of patients with adrenal cortical insufficiency to the metabolic actions of cortisone indicates that care must be employed in its administration to those who are especially sensitive to its stimulatory effects

or who have a prior history of peptic ulcer. Indeed, the pharmacological use of large doses of ACTH, cortisone, or hydrocortisone, for the treatment of inflammatory, allergic, and other disorders may seriously aggravate or induce peptic ulceration even in patients without overt adrenal disease.

Although the presence of an active peptic ulcer does not exclude the existence of Addison's disease, caution in entertaining the diagnosis or in administering cortisone or hydrocortisone to such patients is certainly indicated.

*Kidneys:* Satisfactory demonstration of the kidneys was obtained in 92 patients on routine scout films of the abdomen. In addition, intravenous urography was carried out in 22 cases. Five patients in the group had previously undergone unilateral nephrectomy for renal tuberculosis; the contralateral kidney in these cases showed the expected compensatory hypertrophy. One additional patient possessed a small, diffusely calcified kidney, presumably the result of old tuberculous infection. None of the remaining 86 patients showed evidence of renal tuberculosis either on roentgenograms or by clinical or laboratory examination. This group included 44 males and 42 females. Three of the male subjects, including 2 with roentgenologic evidence of inactive pulmonary tuberculosis, showed renal shadows which were definitely reduced in size. Of the 42 females, only 3 of whom presented evidence of inactive pulmonary tuberculosis, 17 exhibited a significant reduction in kidney size. In 2 patients the kidneys were described as "very small," and in 2 cases they actually decreased in size during the period of observation.

It would appear that renal tuberculosis cannot adequately explain the reduction in kidney size encountered in some patients. In addition the striking sex difference favors an alternative explanation. Since the female patient with Addison's disease is deprived, so far as is known, of the primary source of androgenic hormone, it is tempting to consider the loss of the renotrophic action of this group of steroid agents to be

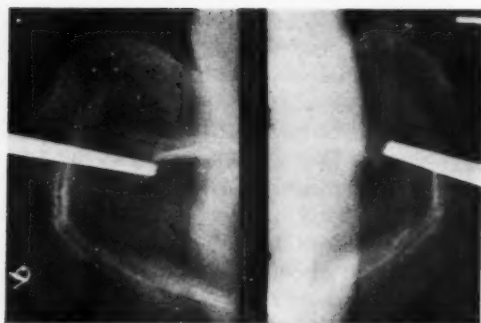


Fig. 7. Ossification of cartilage in the external ears of a patient with Addison's disease.

responsible for the diminished kidney size. It is of interest that a diffuse tubular atrophy has been described (18) in the kidneys of patients with Addison's disease and was present in 2 of the 12 patients in this series examined postmortem. The significance of this lesion is not clear, although it has been attributed to prolonged hypotension and relative anoxemia.

**Sella Turcica:** The sella turcica was normal in 81 patients and at the upper limit of normal size in 4. In the latter cases, there was no evidence of bone destruction or displacement of the clinoid processes. This observation is of importance from the standpoint of differential diagnosis, for absolute sellar enlargement is indicative of the probable existence of an expanding anterior pituitary tumor. In the presence of this finding, therefore, adrenal cortical insufficiency is in all likelihood secondary to anterior pituitary failure. All of the patients in this series were demonstrated to represent primary adrenal cortical insufficiency (absence of ACTH response). It is wise, however, in the first assessment of patients presumed to have Addison's disease to obtain routine skull films. This will aid in identifying the occasional patient with an expanding intrasellar tumor, anterior pituitary insufficiency, and secondary adrenal cortical insufficiency.

**Calcification of the Pinna:** One of the interesting clinical features of many patients with Addison's disease is a sclerotic thickening of the pinna of the ear. In its

early stages, the change is evidenced by a moderate stiffness of the external ear on palpation, not infrequently discovered by the patient himself. In some cases, the abnormality is progressive and may eventually result in the production of an external ear which is stony hard. In these patients, the deposition of calcium in or about the cartilaginous structures of the pinna may be readily demonstrable by x-ray. Six patients in this series had calcific deposits in the pinna which were easily visible on the routine lateral film of the skull, but better visualized with small films placed behind the pinna itself (Fig. 7). In some films a true trabecular pattern indicating the occurrence of metaplastic ossification appeared to be present.<sup>7</sup>

The significance of this unique finding is not clear. Although moderate stiffening of the pinna has been occasionally encountered in previously untreated patients, it would appear to be associated in most cases with prolonged desoxycorticosterone therapy. This is of interest in view of the well known alterations in the structure of intra-articular cartilage produced in animals following the administration of excessive doses of desoxycorticosterone (20). In the present series, however, the appearance of this abnormality is not well correlated with persistent desoxycorticosterone overdosage nor with the presence of articular or vascular lesions which could be attributable to this agent. It may be pointed out that 3 of the 6 patients showing calcification of the pinna revealed progressive and apparently premature calcification of the costal cartilages, suggesting

<sup>7</sup> In this connection, the comments of Batson (25) are of interest: "The cartilages of the external ear are yellow elastic cartilage. Yellow elastic cartilage does not ossify. The question can be raised whether the films of the external ear show calcified cartilage or true bone, the essential difference being whether or not haversian systems are present. This may seem to be a technical problem, but it is significant since calcification in the strict sense is always a pathological process, while ossification is a normal growth process, even though the ossification occurs in an unusual site. Has bone invaded and replaced elastic cartilage, as it does hyaline cartilage, or has bone formed in some adventitious growth of fibrous tissue around the ear cartilages? Heteroplastic growth of bone in normal and abnormal fibrous tissues of the body is well known."



that similar changes in areas less accessible than the external ear, may be present.

The occurrence of calcification of the pinna in a case of acromegaly (26) is of considerable interest in view of the potential synergism assigned by Selye (20) to pituitary growth hormone and desoxycorticosterone in production of lesions of the so-called adaptation syndrome in animals. There is no cogent evidence, however, to suggest an overproduction of growth factor in Addison's disease. Although calcification of the ear has been reported in ochronosis (27), probably secondary to the inflammatory reaction engendered by the deposition of large amounts of melanoid pigment in cartilaginous structures, there is no correlation in patients with Addison's disease between the degree of pigmentation and the amount of sclerosis of the pinna. Furthermore, the deposition of pigment in the pinna is not excessive in comparison to other areas.

*Teeth:* The incidence of dental caries in patients with Addison's disease is strikingly high, and the majority of patients in this series revealed multiple cavities. Except in those instances in which advanced periapical infection was present, the structure of the alveolar process was found to be intrinsically normal and the lamina dura intact.

*Costal Cartilage Calcification:* Due to the interest attached to the presence of abnormal calcification and ossification in the ear cartilage of patients with Addison's disease, it was considered advisable to examine other cartilaginous structures. The costal cartilages were therefore studied in 104 cases by review of the serial examinations of the chest and abdomen. Ninety-three patients showed definite calcification of the costal cartilages (slight 46, moderate 32, and marked 15). Twelve patients revealed no evidence of calcification, of whom 10 were less than twenty years of age. In 15 cases, there was a definite change in the degree of calcification during the period of observation (one to ten years). Since the ages of these patients ranged from nineteen to sixty-nine, the progress of calcifi-

cation was not limited to one specific age group.

The lack of an adequate control series makes the interpretation of these studies difficult, but it is the impression of the authors that the deposition of calcium salts in the cartilaginous structures of these patients may be somewhat more marked than in normals. Whether the calcification bears a significant relation to the type and amount of hormone therapy used is not known.

*Tuberculosis of Bone:* Evidence of tuberculosis of bone was found in 7 cases—in 6 in the lumbar spine and in 1 in the hip joint. The changes in the spine were in all cases far advanced, with marked deformity. It is of interest that only one of the latter group showed calcification of the adrenal glands.

*Osteoporosis:* A moderate degree of generalized osteoporosis was demonstrated in 7 patients, 5 of whom exceeded fifty years of age. This incidence is considered small in view of the relative physical inactivity of a large number of these patients prior to the advent of the highly effective substitution therapy now available. In general, bone structure in patients with Addison's disease was found to be essentially normal.

#### SUMMARY AND CONCLUSIONS

1. Roentgenologic observations in a series of 120 patients with Addison's disease have been described.

2. Adrenal calcification was encountered in 23 per cent of the patients studied. Although its presence is strong presumptive evidence for the existence of adrenal cortical insufficiency, it cannot be considered pathognomonic in view of the demonstration that suprarenal calcification may occur in patients with intact adrenal function.

3. The determination of heart size by teleroentgenography is of value both in the diagnosis of Addison's disease and in the regulation of maintenance hormone therapy. Heart size in untreated, uncomplicated cases is consistently reduced below normal. Following the administration of

adrenal cortical hormones, cardiac dimensions increase and, in the presence of excessive therapy, may considerably exceed normal limits. Therefore, serial roentgenologic measurements of heart size may be extremely useful in the regulation of maintenance hormone treatment.

4. The results of roentgenologic examinations of the chest are in agreement with other evidence that the relative importance of tuberculosis in the causation of adrenal cortical destruction is declining.

5. Other positive findings include: reduction in kidney size, splenomegaly, and calcification as well as ossification in the external ear. The possible significance of these observations has been discussed.

6. It is evident that periodic roentgenologic study of patients with Addison's disease constitutes a useful addition to the effective diagnostic and therapeutic procedures presently available for its control.

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#### SUMARIO

#### Observaciones Roentgenológicas en la Enfermedad de Addison. Estudio de 120 Casos

Las observaciones roentgenológicas descritas versans obre una serie de 120 sujetos que tenían enfermedad de Addison. Descubrióse calcificación suprarrenal en 23 por ciento de ellos. Aunque su presencia constituye poderosa prueba pre-

suntiva de la existencia de insuficiencia corticosuprarrenal, no cabe considerarla como patognomónica, en vista de haberse observado esa calcificación en enfermos que tenían intacta la función suprarrenal.

La determinación del tamaño del cora-

zón por medio de la telerroentgenografía resulta de valor tanto para el diagnóstico como para la comprobación del tratamiento. El tamaño del corazón en los casos no tratados y sin complicaciones está constantemente reducido a menos de lo normal. A continuación de la administración de hormonas corticosuprarrenales, las dimensiones cardíacas aumentan, y si la terapéutica es excesiva, pueden superar considerablemente los límites normales, por lo cual, las mediciones roentgenológicas seriadas del tamaño del corazón pueden resultar sumamente útiles en la regulación de la hormonoterapia.

Otros hallazgos positivos comprenden:

disminución del tamaño de los riñones, esplenomegalia y calcificación así como osificación del oído externo. Discútese la posible importancia de esas observaciones.

Los resultados de los exámenes roentgenológicos del tórax concuerdan con otros datos de que va disminuyendo la relativa importancia de la tuberculosis en la etiología de la destrucción corticosuprarrenal.

Es manifiesto que el estudio roentgenológico periódico de los sujetos con enfermedad de Addison constituye una adición útil a los procedimientos eficaces de diagnóstico y de tratamiento con que ya se cuenta para el dominio de dicha dolencia.

#### DISCUSSION

**Laurence L. Robbins, M.D.** (Boston, Mass.): I doubt if I am the right person to discuss this paper because I do not feel that I am an authority on the subject. This has been, however, an excellent presentation and has covered the roentgen findings of hypoadrenalism better than any I have previously known or heard.

I was glad that emphasis was placed on the increase in heart size while the patient is under therapy. This may be one place where the radiologist can be of considerable help to the clinician, because the increasing size of the heart may be one of the signs that calls attention to the fact that trouble lies ahead. Along with this increase in size of the heart, we have noticed, fluoroscopically at least, a diminution in the amplitude of pulsation. I wonder if Doctor Jarvis would care to say anything as to why this occurs, whether he considers it due to an upset in the chemistries of the heart muscle, retention of fluid within the heart itself, or actual pericardial fluid?

Another important point in early diagnosis is the suspicion of the clinical diagnosis of anorexia nervosa. This may be an early sign of Addison's disease, and any patient with such signs should have thorough study to exclude that condition.

One other question I should like to ask. Has a

sufficiently large number of patients who have shown adrenal calcification without clinical or laboratory manifestations of the disease been studied over a long enough period of time to decide whether they are going to show evidence of adrenal insufficiency? Our experience has been that in these cases adrenal insufficiency does not necessarily develop, but of course most of our patients may have gone over to the Brigham and had the diagnosis established there!

**Dr. Jarvis** (closing): I am sorry I cannot answer Dr. Robbins' question about diminished amplitude of pulsation. There are a number of theories, but the exact cause is not known.

In regard to the presence of adrenal calcification in patients without evidence of adrenal cortical hypofunction detectable by laboratory methods, we have seen four patients, but only one has been followed for six years. Adrenal insufficiency was never demonstrated by laboratory tests. This patient did, however, have clinical signs of adrenal insufficiency, which led to roentgen examination showing adrenal calcification, but in the absence of positive laboratory findings she was not considered to have Addison's disease. As pointed out in our paper, the requirements for a diagnosis of Addison's disease have been quite strict.

## Localization of Intracranial Neoplasms

### with Radioactive Isotopes<sup>1</sup>

WILLIAM B. SEAMAN, M.D., MICHEL M. TER-POGOSSIAN, PH.D., and HENRY G. SCHWARTZ, M.D.,

THE METHOD of detecting and localizing brain tumors by external measurement of radiations emitted by radioactive di-iodo-fluorescein concentrated within the tumor was originated by G. E. Moore and his group at the University of Minnesota in 1947 (3). They first reported on a group of 77 cases, including 49 verified tumors, of which 25 (51 per cent) were correctly localized. A more recent report from this group concerned 26 proved brain tumors from a group of 71 patients studied, of which 17 (65 per cent) were correctly localized (4). The interest in this diagnostic method was heightened by a paper of Ashkenazy, Davis, and Martin (1), who attained an accuracy of 91 per cent in 95 patients with verified brain tumors. Woolsey, Thoma, and Mack (12), using the same method, reported a series of 114 patients with 30 verified brain tumors, of which 24 were correctly localized. Svien and Johnson (8) in a preliminary study found the method approximately 40 per cent accurate. Schlesinger (5), in discussing his experience with 100 cases at the Memorial Hospital in New York, presented no statistical analyses, but emphasized the limitations of the procedure. DeWinter (10), after detecting only 1 out of 20 verified cases, concluded that the method was of little value in tumor localization. Although he used di-iodo-fluorescein, his detecting equipment and method of counting differed markedly from those used by others, which was probably partly responsible for his lack of success.

Radioactive substances other than di-iodo<sup>131</sup>-fluorescein have been tested. Sel-

verstone and Sweet (6) used K<sup>42</sup> for both internal and external localization. With external counting they were able to localize correctly 8 of 10 confirmed supratentorial tumors and none of 5 subtentorial neoplasms. Susen, Small, and Moore (7), also using K<sup>42</sup>, correctly detected 8 of 12 supratentorial tumors, but only 1 of 9 located subtentorially. Apparently heavy concentrations of K<sup>42</sup> in the suboccipital musculature set up a high background which may obscure any differential in radioactivity arising from a posterior fossa neoplasm.

Radioactive iodinated human serum albumin and radioactive sodium iodide (2, 4) have been used more recently by the Minnesota group. Radioactive iodinated human serum albumin is retained in the blood stream longer and permits repeated counts to be made. It has the possible disadvantage of requiring a twenty-four-hour delay after administration before counting can be done, and requires previous treatment with Lugol's solution to block thyroid uptake.

We began using radioactive isotopes to study patients suspected of having organic neurologic disease in January 1951 and have studied 250 patients as of Nov. 1, 1952. Our technic has closely approximated that used by both the Northwestern and Minnesota groups. We are presenting an analysis of our findings in 200 patients studied for a long enough period to permit adequate follow-up and evaluation.

#### INSTRUMENTATION

The scintillation counter used for the radiation detection has been previously

<sup>1</sup> From the Department of Radiology (W. B. S. and M. M. T.) and the Division of Neurological Surgery (H. G. S.), Washington University School of Medicine, St. Louis, Mo. This research was partially supported by the U. S. Atomic Energy Commission and by a Special Research Fund for the Division of Neurological Surgery donated by Mr. George A. Bilgere and Mr. H. Craig Graham.

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described (9). It consists of a detector head containing a scintillation crystal, photomultiplier tube, and cathode follower. The detector head is suspended on a counterbalanced arm which is articulated to allow easy positioning and may be locked in any position by a series of magnetic clutches. The main electronic circuit into which the electrical pulses coming from the cathode follower are fed consists of a linear amplifier, discriminator, integrating circuit, and high-voltage power supply. This transforms the electrical pulses into a direct current whose voltage is proportional to the number of counts recorded by the photomultiplier tube. The counting rate is graphically recorded by an Esterline-Angus chart recorder.

The scintillating element is a single clear sodium iodide (with a small amount of thallium impurity) cylindrical crystal measuring 4 cm. in diameter and 2 cm. in height, which is protected from the air by imbedding in plexiglas. An RCA 5819 photomultiplier tube is used. This set-up results in a counting efficiency of 54 per cent and produces a counting rate of 1,400 counts per second 1 meter from a 1 millicurie source of  $I^{131}$ . It has approximately two hundred times the efficiency of a conventional Geiger tube and about forty times the efficiency of a bismuth-coated cathode Geiger counter.

Before each localization, the counter is standardized with a small radium source and the voltage is adjusted to give a standard counting rate. This calibration is necessary because the counting rate of the instrument is strongly dependent on the voltage between the dynodes, and the reading of the voltmeter cannot be relied upon for proper adjustment.

#### TECHNIC

Di-iodo-fluorescein containing  $I^{131}$  obtained from Abbott Laboratories was used in all patients. The first 22 patients were studied with a bismuth-coated cathode Geiger tube, and in this group the amount of di-iodo-fluorescein injected was 1 millicurie. Because of the greatly increased

sensitivity of the scintillation counter we were able to reduce the dose of di-iodo- $I^{131}$ -fluorescein to 0.25 millicurie in the remaining patients. Following the intravenous injection, the counter is centered over the zygoma and is kept there until the counting rate reaches a plateau, which usually takes fifteen to twenty minutes. Thirty-two positions on the skull are routinely surveyed, including thirteen symmetrical positions on each side and six mid-line positions.

The counter is placed directly on the scalp so that skin contact is maintained. The entire technic, including the counting positions and nomenclature, is essentially the same as that described by Ashkenazy, Davis, and Martin. Because of the high counting rate (600 counts per second over the zygoma twenty minutes after the injection of 250 microcuries), it is necessary to count only fifteen to twenty seconds at each area, thus making possible a complete survey in thirty to forty minutes.

As pointed out by Ashkenazy *et al.*, different locations on the skull normally differ in the concentration of the radioactive isotope. The radioactivity also varies according to the period of time which has elapsed following the injection of the isotope. A difference in counting rate between any two symmetrical areas greater than 10 per cent was considered to be significant, provided it could be obtained on repeated counting. Differences which could not be repeated were frequently due to inaccurate positioning of the counter. The clinical history and findings on physical examination were not given any consideration in the interpretation of the isotope data. A focal lesion was diagnosed only if a differential in radioactivity greater than 10 per cent could be repeatedly demonstrated.

#### RESULTS

Of the 200 cases included in this analysis (Table I), 85 have had surgical or autopsy confirmation. Correct localizations were obtained in 30 of 65 patients with histolog-

ically verified brain tumors, an accuracy of 46 per cent.

TABLE I: CASES STUDIED AND RESULTS

Total patients studied.....	200
Number of verified cases.....	85
Tumors.....	65
Non-neoplastic lesions.....	20
Correct localizations in tumor patients....	30 (46%)
Accuracy in non-neoplastic lesions.....	10 (50%)
Over-all accuracy in verified cases.....	40 (47%)

Twenty non-neoplastic lesions including intracerebral hematomas, aneurysms, and abscesses, were verified. In this group a correct localization of a focal lesion was made in 2 cases of aneurysm of the middle cerebral artery, 1 chronic abscess, and 1 thrombosis of the internal carotid artery. In the remainder of the group, including 1 acute brain abscess and 4 intracerebral hematomas, no evidence of a focal lesion was obtained. The radioactive isotope diagnosis of a localized lesion or absence of a focal lesion was correct in 10 of the 20 non-neoplastic cases, an accuracy of 50 per cent. In the entire group of verified cases, a correct localization of a focal lesion or the correct demonstration of the absence of a focal lesion was made in 40 cases (47 per cent).

In our experience, as well as that of others, subtentorial tumors are notoriously difficult to localize by the isotope method. We were able to localize only 3 of 11 posterior fossa tumors, although one tumor correctly localized was a sarcoma arising in the superior pole of the cerebellar hemisphere, measuring only 2 cm. in diameter. If we exclude the cases of posterior fossa lesions and calculate the accuracy of the method for the supratentorial lesions, we find only a slight improvement in results. Twenty-seven of 54 supratentorial tumors were correctly localized, an accuracy of 50 per cent (Table II).

A study of the incidence of the various histologic types of tumor in both the correctly and incorrectly localized groups reveals that the meningioma is the most favorable tumor for this method of localization. Eleven of 12 meningiomas were correctly localized, the exception being one situated in the posterior fossa (Table III).

Only 3 of 9 astrocytomas, 4 of 11 metastatic carcinomas, and 6 of 16 glioblastomas multiformes were correctly localized.

In the remaining 116 unverified cases, there were 21 instances of radioactive isotope localization. Two of these were in patients with previously verified brain

TABLE II: ANALYSIS OF RESULTS ACCORDING TO LOCATION OF TUMOR

Supratentorial tumors	
Total.....	54
Correctly localized.....	27 (50%)
Missed.....	27
Posterior fossa tumors	
Total.....	11
Correctly localized.....	3 (27%)
Missed.....	8

tumors and probably represented residual or recurrent tumor. Since we were unable to obtain histologic verification subsequent to the isotope study, these were not considered confirmed cases. Two localizations were obtained in patients with proved metastatic cancer elsewhere in the body,

TABLE III: HISTOLOGIC TYPES OF VERIFIED TUMORS

	No. Correct	Total No.
Meningioma.....	11	12
Astrocytoma.....	3	9
Metastatic carcinoma.....	4	11
Glioblastoma multiforme.....	6	16
Undifferentiated glioma.....	0	3
Pituitary tumor.....	0	2
Hemangioblastoma.....	0	2
Ependymoma.....	0	2
Miscellaneous.....	6	8
	30	65

probably indicating the correct localization of cerebral metastases. Nine patients had normal ventriculograms or encephalograms following positive isotope localization. These probably represent false localizations, although we do not believe that a normal ventriculogram always excludes the presence of an intracranial tumor. Focal vascular or demyelinating lesions will also cause localized concentration of di-iodo-fluorescein. If lesions of this type are diffuse and generalized, an abnormally high general level of radioactivity will result without localization. One of the highest counting rates we have ever recorded was obtained in a case of acute multiple sclerosis which was subsequently confirmed at autopsy.

It is noteworthy that no localization was obtained in 4 instances of verified extracranial tumors, including 2 metastatic tumors of the scalp, a malignant orbital tumor arising from the lacrimal gland, and a myeloma involving the petrous bone, even though the superficial lesions were very close to the scintillating crystal. Correct localization was obtained in a patient with a chondrosarcoma arising in the nasopharynx and invading the base of the brain. In one of the patients with metastasis to the scalp, we obtained a successful localization of an intracerebral metastasis even though the extracranial metastasis exhibited no evidence of radioactivity. These data support the contention that isotope localization is probably not specific for tumor tissue but merely indicates an area of brain tissue where the blood-brain barrier has been sufficiently altered to permit extravasation of the isotope.

#### LIMITATIONS

With the method and instrumentation outlined above, the localization of a tumor containing a high concentration of a radioactive isotope is not based on directional collimation of the detecting element but rather on the proximity of the isotope concentration to the radiation detector. Under such conditions, the superficial location of a tumor results in the greatest differential of radioactivity and a centrally placed lesion might result in no differential. Very small tumors may also be missed unless they happen to have a very high differential absorption ratio for the isotope used. Biological factors such as extensive necrosis and/or cyst formation result in little or no concentration of the isotope in the lesion.

Upon reviewing the tumors that we failed to localize, we found that about two-thirds of them possessed biological and/or physical characteristics that could account for their failure to be localized. Most of those listed in Table IV were cystic as well as necrotic, including the 2 pituitary tumors. For similar reasons, Svien and Johnson estimate that this method of tumor

TABLE IV: BIOLOGICAL AND PHYSICAL CHARACTERISTICS OF THE TUMORS NOT LOCALIZED

Cystic tumors.....	6
Necrotic.....	8
Mid-line.....	7
Small (less than 2 cm.).....	2
TOTAL.....	23

localization is applicable in only 50 per cent of brain tumors. The latter workers interpreted their studies as indicating that the differential retention of di-iodo-fluorescein was a function of the degree of cellularity of the tissue involved, and independent of whether or not the cells were malignant. Ashkenazy, Davis, and Martin believe that the affinity of the isotope for tumor tissue is related to the cellularity and vascular pattern and that, therefore, the more malignant neoplasms show a greater uptake. The histologic sections of our tumors were reviewed by Dr. D. E. Smith of the Department of Pathology, who attempted to grade them according to their cellularity, vascularity, and extent of the microscopic necrosis. We could find no striking correlation between these factors and the ease or failure of localization.

#### CLINICAL ROLE OF ISOTOPE ENCEPHALOMETRY

We have compared the accuracy of our di-iodo-fluorescein studies to that of the electroencephalogram in the same patient. In 50 patients both radioactive isotope and electroencephalographic studies were done. Twenty-four (48 per cent) of these were correctly localized by the latter procedure, while 23 (46 per cent) were correctly localized by the isotope method. Further analysis reveals that in a group of 23 cases in which the radioisotope studies were correct, successful electroencephalographic localization occurred in only 10 instances, while in 27 cases in which the lesion was missed by the isotope method, correct electroencephalographic localizations were obtained in 14. This suggests that the two methods may be somewhat complementary so far as the localization of brain tumors is concerned.



Fig. 1. Case G. S. Roentgenogram of the orbits showing a homogeneous increase in density and thickening of the greater and lesser wing of the left sphenoid bone.

It is difficult to determine the clinical value of this method in view of the rather significant incidence of what are probably

false positive localizations in the unverified cases. Some of these could represent small tumors or focal areas of encephalitis or vascular lesions. A definite localization may always indicate an area of abnormal brain, although the specific abnormality may not be a neoplasm. The procedure may be a useful screening process to aid in the selection of patients for further diagnostic studies such as arteriography and ventriculography. The following brief case report exemplifies this aspect of clinical utilization.

#### CASE HISTORY

For the past ten years a 48-year-old white woman had noticed gradual progressive proptosis of the left eye associated with diminution in vision and a dull aching pain inside the orbit. Examination revealed a moderate proptosis of the eye, optic atrophy, and prominence of the left frontal bone and lateral orbital wall. Roentgenograms disclosed a diffuse increase in thickness and density of the lesser and greater wing of the sphenoid on the left (Fig. 1). The roentgenographic appearance plus the long duration of the symptoms favored a diagnosis of fibrous dysplasia, although the possibility of a meningioma could not be excluded. A di-iodo-fluorescein study showed a marked concentration of radioactivity in the left frontal area. This study was followed



Fig. 2. Case G. S. Arteriogram demonstrating upward and medial displacement of the left middle cerebral artery. The anterior cerebral artery is pushed posteriorly and across the mid-line.

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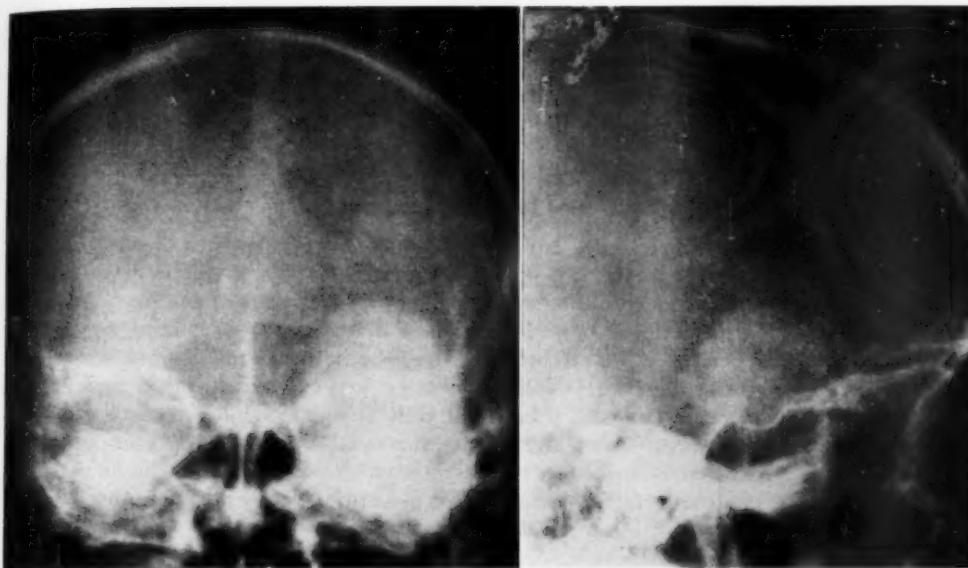


Fig. 3. Case G. S. Arteriogram a few seconds later than Fig. 2, showing complete opacification of a sphenoid wing meningioma.

by cerebral arteriography, which demonstrated marked displacement of the middle cerebral artery and opacification of a large tumor of the left sphenoidal wing (Figs. 2 and 3). Histologic examination of the excised tumor proved it to be a fibroblastic meningioma.

#### CONCLUSIONS

1. Our clinical experience with the di-iodo-fluorescein technic of brain tumor localization in 200 patients has been presented. A correct localization was obtained in 46.0 per cent of 65 verified brain tumors.

2. Failure to localize a tumor may be the result of an unfavorable location or of biologic characteristics that interfere with the basic mechanism of localization of the medium.

3. The clinical status of this test is yet to be definitely determined, but we feel that it is a useful screening procedure to aid in the selection of patients for further diagnostic studies.

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# SUMARIO

## Localización de las Neoplasias Intracraneales con Isotopos Radioactivos

A 200 enfermos que tenían lesiones intracraneales sospechosas se les examinó por medio de un cuentachispas a continuación de la inyección intravenosa de bi-yodo-fluoresceína. Reconociéronse metódicamente treinta y dos sitios del cráneo, colocando el cuentachispas directamente sobre el cuero cabelludo. Se aceptó como significativa toda diferencia en la medición de la velocidad entre cualesquiera dos zonas simétricas que excedía de 10 por ciento y sólo se diagnosticó lesión focal cuando podía observarse repetidamente una diferencia de dicha magnitud en la radioactividad presente.

Ochenta y cinco casos de la serie fueron comprobados al operar o en la autopsia. Obtuvieron localizaciones exactas en 30 de 65 enfermos que tenían tumores cerebrales comprobados y en 10 de 20 que tenían lesiones no neoplásicas. Resultó más difícil localizar los tumores de la fosa posterior que los supratentoriales, repre-

sentando los porcentajes de localización acertada 27 y 50 por ciento para los dos grupos, respectivamente. De las varias formas histológicas, los meningiomas acusaron los resultados más favorables.

Entre los 115 casos no comprobados, hubo 21 de localización radioactiva. Nueve de éstos se considera que representan seudopositivas, dado que los subsiguientes hallazgos ventrículo- o encefalográficos fueron negativos.

Es difícil determinar el valor clínico de la localización de las lesiones cerebrales con isotopos radioactivos, sobre todo vista la incidencia bastante elevada de probables positivas falsas en el grupo sin comprobar. Es posible que, en algunos de éstos, tal vez existieran pequeños tumores o zonas focales de encefalitis o lesiones vasculares. El método se considera útil como procedimiento de tria para ayudar en la selección de los enfermos destinados a ulteriores estudios de diagnóstico.

# DISCUSSION

**Laurence L. Robbins, M.D.** (Boston, Mass.): As my contact with this field has been largely that of an onlooker, I went over this paper very thoroughly with Dr. William Sweet of our Department of Neurosurgery, as he and his associates have done most of this type of work.

Dr. Sweet's conclusions are much the same as those of Dr. Seaman and his group, that their results have been disappointing. They have used potassium 42 to a considerable degree and have found that abnormal brain tissues, *i.e.*, neoplastic tissue, will pick up the potassium at a ratio of 10 to 150 times normal brain tissue. They have been able rarely to localize a tumor which was not demonstrable by other more ordinary means or more frequently used methods such as encephalography, ventriculography, and arteriography. Dr. Sweet and his associates are now investigating the use of positron-emitting isotopes—copper 64, manganese 32, and arsenic 74—but as yet they have not been satisfied with their results.

The authors of this present paper are to be congratulated on their very fair and honest appraisal of the method—a method which undoubtedly in the past has been received over-enthusiastically but is now beginning to find its level. Though it offers an additional means of searching for a brain tumor, it certainly stands in need of further investigation.

**Dr. Seaman (closing):** I would like to thank Dr. Robbins for his remarks and say that we agree. Among our 250 cases I can think of only one, perhaps two, in which the isotope data gave us information which is not readily obtained by other more conventional means such as ventriculography, clinical examination, and electroencephalography. On the whole, however, the procedure has been found to be helpful and useful. When the observations are interpreted in the light of clinical data, it might also be of value in non-neoplastic conditions.

## Changes in the Central Nervous System Following Irradiation with 23-mev X-Rays from the Betatron<sup>1</sup>

A. ARNOLD, M.D., P. BAILEY, M.D., R. A. HARVEY, M.D., L. L. HAAS, M.D., and J. S. LAUGHLIN, Ph.D.

**D**URING THE PAST three years, studies have been in progress to determine and analyze the effects of x-rays on the normal brain of the monkey and on tumors of the central nervous system of man. Although these studies have been carried out primarily with 23-mev x-rays, produced by the University of Illinois betatron, additional comparative studies utilizing 200 and 400 kv. x-rays have also been undertaken. Our findings, to date, would indicate that the brain of both monkey and man is more radioresponsive than previously supposed, and that the pathological changes produced by these radiations are due to a direct effect upon the neural elements. These observations are definitely contradictory to the observations made by previous investigators (1-5) who have irradiated the central nervous system of a variety of animal species, including man (6). In general, these authors have concluded (a) that the central nervous system is highly radioresistant, in that it requires many thousands of roentgens to produce any recognizable pathological effects, and (b) that any changes produced by the radiations are secondary to an interruption of the vascular bed rather than to a direct injurious effect upon the neural elements. An exception to the second concept was made by Davidoff and co-workers (7), who exposed the brains and spinal cords of the adult monkey (*Macacus rhesus*), through an open wound, to single doses of 200 kv. x-rays, from 1,000 to 5,000 r (as measured in air), and demonstrated that the nervous and glial cells were affected, whereas the changes in the blood vessels were surprisingly slight in degree. With reference to the human brain, O'Connell and Brunschwig (8) and Wachowski and Chenault (9)

noted, in their patients receiving x-ray therapy, that the radiation produced changes in both the neural elements and some of the vessels but that the neural changes were primary effects rather than a result of the vascular changes noted.

In addition to our observation that the central nervous system is more radioresponsive and that the neural elements respond directly to the radiation, we have noted a very striking selective destruction of the white matter occurring months to a year or more after irradiation. This readily demonstrable radioselectivity for the white matter begins as a demyelinating process and proceeds, with time and increasing dose, to an actual necrosis of the myelin and axons, whereas, in comparison, the irradiated neurons show only moderate changes. This phenomenon of delayed radionecrosis of the white matter is not related to the occlusion of vascular channels, but is due to an actual destruction of the myelin and axons. It has appeared in our experimental animals, as well as in our patients with neoplasms who have received x-ray therapy with either the betatron or with standard x-ray machines of lower energies.

This problem of radionecrosis is of extreme importance in planning the therapy of brain tumors, particularly those along the central axis of the brain, since both our experimental animals and some of our patients are showing extensive destruction of the vital centers in the hypothalamus and brain stem following irradiation. The tumor dosages employed in our patients have been less than the acceptable dose of 6,000 r given by some therapists for tumors of the central nervous system. This frequently applied maximum dose is based

<sup>1</sup> From the Department of Neurology and Neurological Surgery and the Department of Radiology, University of Illinois College of Medicine, Chicago, Ill. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

This work is supported by a grant from the U. S. Public Health Service.

on the concept that the nervous system is strongly radioresistant, a concept which we believe is quite erroneous.

#### EXPERIMENTAL PROCEDURE

Healthy adult monkeys (*Macaca mulatta*) of both sexes, weighing 2.5 to 4.0 kg., were exposed under Nembutal anesthesia to single total doses of 23-mev x-rays from the betatron, via a 1.0 or 2.5 cm. circular port, transtemporally or transfrontally. To date, a rather wide range of single doses of x-rays from 1,500 to 14,000 r has been studied. Additional animals will be given doses of 750 r and 375 r to determine the effects at these very low levels. The range of dosage employed, 1,500 to 14,000 r of 23-mev x-rays as delivered by the betatron, is equivalent to 900 to 8,400 r of 250-kv. x-rays, utilizing the conversion factor of 0.60, which is the approximate factor<sup>2</sup> for the biological effectiveness of 23-mev x-rays (10-13). The rate of irradiation with the 1.0-cm. beam was 150 r/min.; with the 2.5-cm. beam, 75 r/min. No filter was employed with the 1.0-cm. beam, whereas a compensating filter was used in the 2.5-cm. beam. In all cases, the target-skin distance was 83.4 cm.

For the actual radiation exposure, the monkey's head was held horizontally by means of a specially devised holder, so that the entry portal of the beam was in the right temporal or frontal region and the exit portal was in the left temporal or frontal region, respectively. A 3.4-cm. block of lucite was placed against the right side of the head in order to increase the intensity of ionization to the 100 per cent peak of the dose-distribution curve. Since the dose-distribution curves of the 1.0-cm. and 2.5-cm. beams of 23-mev x-rays have, at their peak intensities, a nearly flat plateau of 95 to 100 per cent ionization for the next 4.5 cm. of tissue penetration, and since the average transfrontal and transtemporal diameters were 5 cm. in the monkeys selected for irradiation, it was possible to maintain a fairly uniform tissue-

dose distribution through the brain. By actual determination, the entry skin dose was 100 per cent of the maximal dose, and the exit skin dose was 95 per cent of the maximal dose. This uniformity of dose distribution obtainable with the betatron at the maximum ionization plateau of the 1.0-cm. and 2.5-cm. beams made it possible to detect bilateral areas in the brain of comparable radioresponsiveness. In addition to the experimental advantage of the betatron in delivering a more uniform tissue dose, the 1.0-cm. and 2.5-cm. beams of x-rays used remained so well collimated, without significant side-scattering, that the area of epilation on the exit side was no more than a millimeter greater in diameter than the epilated area at the entry side.

Following the administration of the selected total dose of radiation at a single exposure, each monkey was carefully observed for any clinical evidence of irradiation damage. The animals were then sacrificed at intervals after radiation, particularly when they showed evidence of radiation injury. For this present report, the longest period of observation after irradiation was twelve months; additional monkeys are being observed for a period of two years. The brains were perfused with 10 per cent formalin via the carotid arteries after preliminary washing with isotonic saline solution, and were fixed in large volumes of 10 per cent formalin for ten days to two weeks and imbedded in celloidin. The entire brain was then serially sectioned at 20 microns. Each 20th section was saved, beginning with the 20th, 21st, and 22nd, and Nissl, Weil-Van Gieson, and hematoxylin-eosin preparations made. A number of monkeys died during the first few days after irradiation, particularly those exposed to the larger, lethal doses of x-rays with the 2.5-cm. beam. Additional monkeys were allowed to go through the entire period of delayed radionecrosis in order to determine the lethal effect of the dose administered. Death usually followed even the lowest doses when the radiation traversed vital areas in the brain stem and hypothalamus.

<sup>2</sup> The exact factor for the biological effectiveness of 23-mev x-rays is as yet in dispute.



TABLE I: SPECTRUM OF RADIATION EFFECTS AS RELATED TO SINGLE TISSUE DOSES OF 23-MEV X-RAYS

Dosage		Acute Effects	Intermediate Effects	Late Effects
1. 23-mev rays (betatron)	2. 250 kv. rays*	1 day to 4 weeks	1 to 4 mos.	5 mos. and longer
1. 7,000-14,000 r		Acute necrosis		
2. 4,200-8,400 r				
1. 5,000-7,000 r		Acute inflammation	Partial recovery	Delayed radionecrosis
2. 3,000-4,200 r		Hemorrhages		
		Partial necrosis		
		Edema		
1. 3,000-5,000 r		Acute inflammation	Complete recovery	Delayed radionecrosis
2. 1,800-3,000 r		Hemorrhages		(selectivity for myelin)
		Edema		
1. 1,500-3,000 r		Acute inflammation	Complete recovery	Delayed radionecrosis
2. 900-1,800 r				(selectivity for myelin)

\* Converted dose based on biological effectiveness.

The choice of utilizing a small 1.0-cm. or 2.5-cm. beam of x-rays, rather than carrying out total irradiation of the head, was made so that sufficient non-irradiated brain would be available as a histologic control for the irradiated areas. The average dimensions of the brains of the monkeys used in this series were: 6.0 cm. fronto-occipital diameter, 4.0 cm. transtemporal diameter, and 3.2 cm. vertex-to-base diameter. For those monkeys exposed to the 1.0 cm. beam of radiation, therefore, there was 5.0 cm. of non-irradiated tissue in the fronto-occipital diameter, and 2.2 cm. of tissue in the vertex-to-base diameter, for control examination. The monkeys irradiated with the 2.5-cm. beam had 3.5 cm. of non-irradiated tissue in the fronto-occipital diameter and 0.7 cm. of tissue in the vertex-to-base diameter for histologic control. By thus using each monkey as a control for its own irradiated area of brain, it was possible to rule out postmortem changes and artefacts, and to detect the early changes leading to delayed radionecrosis. The neurologic comments in this report are based upon 60 irradiated monkeys, whereas the actual histologic findings are from an analysis of some 10,000 sections of the first 25 brains, prepared as outlined above.

#### RESULTS

Table I shows the pathological findings observed in our animals, as related to the specific tissue dose of 23-mev x-rays ad-

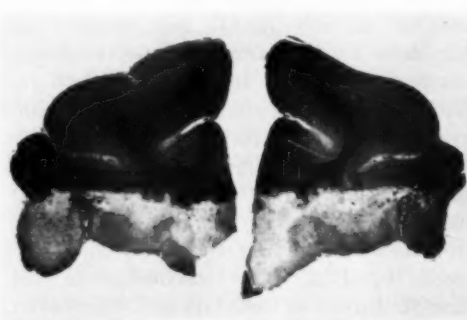


Fig. 1. Acute radionecrosis of the bases of the frontal lobes of a monkey produced by a single dose of 7,000 r.

ministered. Beneath each dose of 23-mev x-rays, the equivalent dose of 250-kv. x-rays is given. A conversion factor of 0.60 was used in determining these equated dosages, since the r as delivered by the betatron at an energy of 23 mev is about 40 per cent less effective, biologically, than the r as produced by the conventional x-ray machine at 250 kv. (10-13).

Single tissue doses of 7,000 r or more produced an acute necrosis of the entire area of the brain traversed by the beam of x-rays. At this dose range, there is no evidence of radiosensitivity. Figure 1 is a coronal section through the frontal lobes of a monkey that had received 7,000 r along the base of its frontal lobes with the intent of producing a frontal lobotomy. This was obviously accomplished, and the monkey remained lobotomized, clinically (lack of interest in surroundings, slowed responses, apathy, etc.), up to the time of

sacrifice. Such large tissue doses, 7,000 r or more, given in a single exposure were not incompatible with survival of the animal, provided the radiation traversed only cerebral cortex, and not the brain stem or hypothalamus. These latter structures appeared to be particularly vulnerable to the effects of radiation.

In the dose range of 5,000 to 7,000 r the acute pathological findings were inflammatory reactions, edema, myelin injury, hemorrhages, and occasional small areas of acute necrosis. The inflammatory responses, edema, and hemorrhages slowly resolved in the ensuing weeks, but the areas of necrosis persisted. All the monkeys in this dose range showed extensive clinical manifestations of irradiation, such as quadriplegias, generalized seizures, and reductions of the state of consciousness. These clinical findings became apparent upon recovery from the anesthetic, or appeared very rapidly within the first twenty-four hours after the radiation had been given, reaching their maximum intensities at three to four days. Thereafter, the seizures subsided and a more normal state of alertness returned. The quadriplegia, in each instance, improved much more slowly, so that by the end of two weeks or more a moderate quadriparesis with hyperreflexia was still evident. By four to five weeks post-irradiation, all evidence of muscular weakness was gone, and all the monkeys were well, clinically, with the exception of an occasional animal which showed a persistent hyperreflexia beyond the acute period. This persistent hyperreflexia could be related to the small areas of acute necrosis, occurring in the upper limits of the dose range of 5,000 to 7,000 r. The majority of the monkeys, however, upon recovery from their acute neurological syndrome, remained well clinically for a period of four months or longer. There then appeared, rather abruptly, at this late stage, a number of intense and rapidly progressive neurological disorders due to *delayed radionecrosis*. Monkeys that had been physically well and neurologically negative during the

intermediate period now became rapidly apathetic and quadriparetic. Within a period of ten days to two weeks these animals grew rapidly worse and became quadriplegic and comatose, and eventually expired. Microscopic examination revealed extensive non-selective radionecrosis throughout the entire path of the beam, and only in the path of the beam.

In the dose range of 3,000 to 5,000 r, the clinical defects, which were also apparent following recovery from the anesthetic, were less severe than those observed in the monkeys receiving the higher doses of x-rays. There appeared in these animals a definite reduction of the level of consciousness, occasional generalized seizures, and a mild quadriparesis, with an associated hyperreflexia. These acute clinical signs usually subsided within the first weeks, so that each monkey shortly regained its pre-irradiation level of alertness and muscle strength. In an occasional monkey, the hyperreflexia tended to persist for an additional week, but thereafter all monkeys in this dose range remained neurologically normal until the onset of delayed radionecrosis, some six to eight months later. Histologic examination of the brains of the monkeys sacrificed during the acute stage of the reaction following 3,000 to 5,000 r revealed intense inflammatory reactions, hemorrhages, myelin damage, and edema throughout the irradiated part of the brain. It should be pointed out at this time that some of the acute inflammatory cellular reactions spread beyond the specifically irradiated area, producing a moderately diffuse meningo-encephalitis. This diffuse meningo-encephalitis appeared to be responsible for the generalized seizures and the depression of the level of consciousness observed in all of our monkeys during the acute stage. The inflammatory process was more extensive with the larger 2.5-cm. beam of x-rays, and it was more intense with the higher doses administered.

Patients receiving courses of x-ray therapy for neoplasms of the brain frequently show an aggravation of symptoms, plus

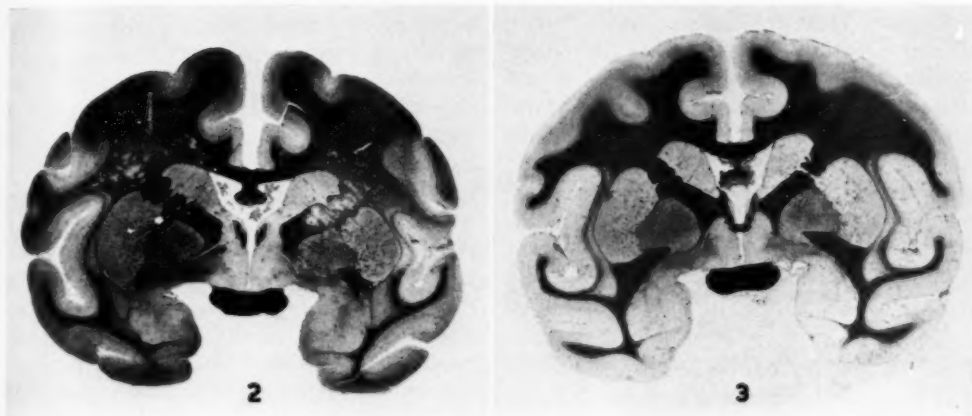


Fig. 2. Delayed radiation effect appearing six months after irradiation.  
Fig. 3. Section of a non-irradiated monkey at the same level, for comparison.

headaches, nausea, and vomiting (radiation sickness), during treatment. This phenomenon of radiation sickness can now best be explained by two factors: (1) the acute inflammatory reactions and edema of the specific area irradiated and (2) the diffusion of the inflammatory reactions beyond the irradiated area so as to give rise to an acute meningo-encephalitis. This spreading inflammatory process was maximum in the areas closest to the area irradiated.

Those monkeys that received 3,000 to 5,000 r were well in all respects during the intermediate period. Animals sacrificed during this period showed only minor nervous and glial cell changes, which will be described in greater detail in a future report. These cellular alterations were present only in the pathway of the beam and would have been difficult to detect had there not been considerable non-irradiated control areas in the same and adjacent brain sections for comparison. Essentially, therefore, these monkeys showed a virtually complete recovery during the intermediate stage, followed some six to eight months later by a less fulminating course of delayed radionecrosis which was strikingly selective for the white matter. This delayed radiosensitivity for the white matter occurred only in the irradiated area, never extending beyond the limits

of the beam of x-rays employed. The changes in the neurons were slight in comparison to the destructive changes appearing in the white matter. Figure 2 shows such a delayed radiation effect on the white matter, while Figure 3 is a control slide from a non-irradiated monkey for comparison. The section shown in Figure 4 demonstrates areas of comparable radiosensitivity in the white matter; Figure 5 is a control slide from a non-irradiated monkey, at the same level of section, for comparison.

The disintegration of the white matter began as a demyelinating process and progressed to an actual necrosis of the white matter constituents, *i.e.*, the myelin, glial cells, and axons. Reparative processes were not particularly active or extensive, as only a rather moderate gliosis and fibrosis occurred in the tissues surrounding the areas of necrosis. This would indicate a definite impairment of the reactivity of the glial cells by radiation. This breakdown of the white matter appears to be a degenerative effect of the radiation. No vascular occlusions were observed and, although there eventually appeared some mild thickening of a few of the vessels, the process of demyelination appeared before the occurrence of any vascular changes.

The pattern of post-irradiation reactions of the monkeys in the dose range of 1,500

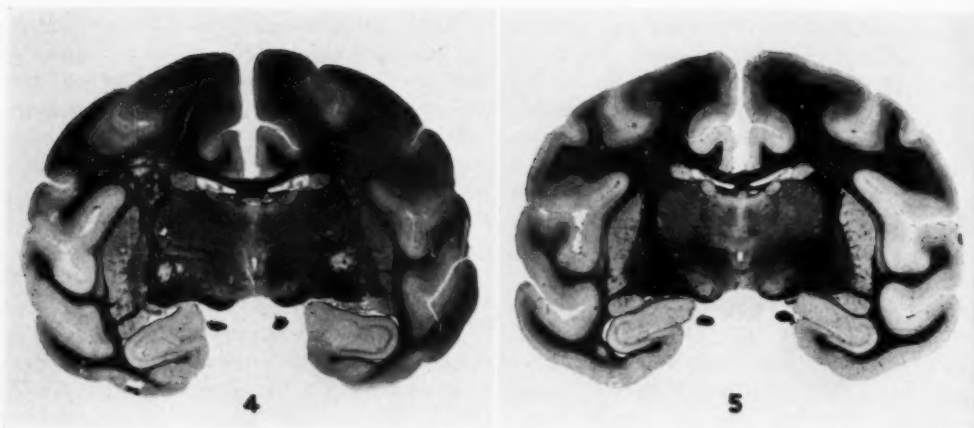


Fig. 4. Areas of comparable radio-responsiveness in the internal capsules and deep cortical white matter of both hemispheres.

Fig. 5. Section of a non-irradiated monkey at the same level, for comparison.

to 3,000 r was less intense but otherwise identical with the reactions observed in the dose range of 3,000 to 5,000 r.

#### DISCUSSION

The evaluation of the effects of radiation on any normal tissue is difficult, and this is particularly so for the central nervous system. Many of the previous investigators who have studied the effects of x-rays upon the intact central nervous system failed to examine the irradiated tissues at sufficiently frequent intervals over a prolonged period of time after irradiation, and thereby failed to observe the entire sequence of pathological events that may occur. It is rather interesting to note that the histological examinations were frequently performed during the intermediate period, when an almost complete recovery can occur from the intense, acute effects of radiation. As the result of such negative findings, the authors of such studies have labeled the central nervous system as being radioresistant. We believe that this concept is erroneous, and that it can be shown that the central nervous system is actually responsive to lower doses of x-rays. It is very probable that the acute responses, as well as the late responses, will occur with lower dosages of x-rays than those we have given, but it may be neces-

sary to observe the irradiated animal for at least two years or more for the appearance of the delayed response.

The demonstration that 7,000 r or more of 23-mev x-rays on the monkey will produce acute necrosis of the frontal lobes suggests the possibility of utilizing radiation as a means of performing frontal lobotomies. Monkeys will certainly tolerate large single doses of x-rays, provided the size of the beam is kept small and vital areas such as the brain stem and hypothalamus are avoided. This may be true for the brain of man as well, but the specific dose of x-rays required for such an effect remains to be determined.

The appearance of delayed radionecrosis in the monkey following single doses of x-rays as low as 1,500 r does not in any way imply that such a phenomenon will occur with a tumor dose of 1,500 r given in a fractionated course to a patient with a brain tumor. However, we have observed a number of patients in whom delayed radionecrosis occurred a year or more after irradiation, following a tumor dose of 4,000 r of 250-kv x-rays given in one or more well fractionated courses, and following a tumor dose of 6,000 to 7,500 r of 23-mev x-rays, given in one fractionated course. Since the predominant feature of delayed radionecrosis is a disintegration of



the white matter, and inasmuch as most of the gliomas of the cerebral hemisphere are subcortical in position, it may be therapeutically advisable to give a large specific tumor dose to destroy the more malignant cortical gliomas and then, should a delayed radionecrosis appear in the irradiated cortical region, to remove the radionecrotic area surgically and thereby salvage the life of the individual. Such a therapeutic procedure would, of course, produce a considerable neurological deficit in most patients, but in some with neoplasms in the more silent areas of the cortex such a deficit would be minimal. On the other hand, patients with neoplasms along the central axis of the brain will definitely not tolerate high doses of x-rays and it becomes essential, therefore, to determine an optimal tumor dose which will inhibit the growth of the more or less radioresponsive tumors occurring in the brain stem and hypothalamus of man, without the production of deleterious changes in these vital areas.

Certainly, the problems in the therapy of patients with neoplasms of the central nervous system are many and will require years of effort for solution. We do hope, however, that such experimental analyses of the effects of radiations on the central nervous system of man and animals as we have undertaken will yield data to aid and guide us in the treatment of those unfortunate individuals afflicted with neoplasms of the brain.

#### CONCLUSIONS

Studies were undertaken to determine and analyze the effects of x-ray irradiation in the normal brain of the monkey and on tumors of the central system in man. The following conclusions were reached:

1. The central nervous system of both monkey and man is more radioresponsive than generally supposed.
2. The effects of x-rays on the central nervous system are direct effects, and are not secondary to vascular occlusion.

3. There is a very definite radiosensitivity on the part of the white matter in the adult animal, which is characteristic for the delayed response in the lower dose ranges.

4. Comparable radiation effects are being observed in our patients receiving x-ray therapy for tumors of the central nervous system.

Specific tumor doses which will either inhibit or destroy the various tumors of the central nervous system of man, without producing late deleterious brain damage, are being determined.

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#### SUMARIO

#### Alteraciones del Sistema Nervioso Central Consecutivamente a la Irradiación con Rayos X de 23-mev Procedentes del Betatrón

Expusieron monos normales a dosis totales únicas de 23 mev de rayos X procedentes del betatrón, de tal modo que la puerta de entrada del haz de rayos quedaba en la región temporal o frontal derecha y la de salida en la región temporal o frontal izquierda, respectivamente. Se usaron haces de 1.0 y 2.5 cm., para dosis totales de 1,500 a 14,000 r, representando de 900 a 8,400 r de radiación de 250 kv. El tejido cerebral no irradiado de cada animal sirvió de testigo para las observaciones realizadas en la zona irradiada. Sesenta animales fueron sometidos a observación en cuanto a los efectos neurológicos de la irradiación.

Los hallazgos discreparon de los obtenidos por investigadores anteriores, quienes han sostenido que el tejido nervioso central es resistente a la irradiación. Por el contrario, se observó radiorreactividad bien definida, demostrándose además que las alteraciones inducidas por la irradiación representan un efecto directo sobre los elementos neurales.

Notóse radionecrosis tardía consecutivamente hasta a dosis de no más de 1,500 r. Dosis de 7,000 r o más no fueron incompatibles con la sobrevivencia con tal que los rayos no atravesaran el tallo cerebral y el hipotálamo, órganos estos que parecían ser en particular vulnerables a los efectos de la irradiación. Las dosis de esa escala elevada fueron seguidas de signos clínicos de lobotomía, que persistieron hasta que se sacrificó el animal. Se produjo una necrosis aguda de toda la zona irradiada.

Con dosis más bajas, un período de respuesta clínica aguda fué seguido de reposición aparente, suplantada al cabo de algunos meses por trastornos neurológicos de rápido avance, debidos a radionecrosis retardada. Con dosis de 5,000 r o menos, hubo radioselectividad bien definida para la sustancia blanca del cerebro irradiado.

Se han observado efectos comparables en enfermos que recibieron roentgenoterapia para tumores del sistema nervioso central.

#### DISCUSSION

**Roger A. Harvey, M.D.** (Chicago, Ill.): Even though the x-ray beam from the betatron has not created any specific differences in cellular responses from those one is accustomed to see with conventional voltage therapy, I am sure you will all agree that the betatron has given stimulus to fundamental research in radiobiology.

The paper this morning is just one example of what is going on in our institutions under the stimulus of the betatron. Dr. Arnold's description of the adequacy of the blood supply following heavy doses of irradiation to the central nervous system may be a surprise to some of you, but is additional confirmation of observations that are being made with increasing frequency in other areas of the body. Dr. Roswit reported in October, at the

annual meeting of the American Cancer Society in New York, on his studies of circulation time in skin in heavily irradiated areas. He found that the circulation time in irradiated skin and control skin was identical or approximately identical. Here, in the central nervous system, we think we have another indication that the blood supply may be adequate in spite of our previous concepts.

Dr. Arnold's initial conclusions are certainly valuable and may well be the basis for specific revision in our idea of the relative sensitivity of neurotissue to irradiation. This has been suggested by other workers in the past, but apparently has never been accepted by the general reviewers, who still hold that the late effects are due to vascular inadequacy.

As a matter of practical understanding and possible application of some of the observations made this morning, I would like to show you some clinical examples of late radiation damage. First, I would urge upon the clinical radiologists here, and also the physicists, the importance of a decision, in each case in which treatment is undertaken, as to whether palliation or cure is to be attempted. In the curative cases, you are going to run the chance of encountering these late necroses, and I think we are going to have to adopt new methods of handling them.<sup>1</sup>

Our first slide shows an isodose curve which I think many of you will recognize as having been published previously. It is on a patient with a glioma of the frontal lobe. You will note that, in treating this patient with the betatron, we were able to use a large number of ports of entry, that there is a superficial sparing, and that there is also a very definite advantage in the concentration of dose in the tumor area. This patient did very well for thirteen months and then began to deteriorate rapidly, with signs of increased intracranial pressure. We were asked to give him additional treatment on the basis that he had either recurrent or residual tumor. Fortunately, he went downhill so rapidly that we were not forced to make the mistake of giving further irradiation.

At autopsy, a cross section of the brain through the mid-tumor area showed an area of what might be mistaken for tumor but was in fact necrotic brain tissue. You will notice how this whole hemisphere is swollen and would account for the increased intercranial pressure. Actually this area was very soft and necrotic appearing, and Dr. Arnold made the comment then that, had he been aware of the true situation, he would have explored this patient and sucked out the necrotic mass.

Even at this stage of fixation, the vascular prominence throughout this zone is evident; microscopically there is a severe degree of demyelination going on. In a section obtained from farther back in this same brain one sees a rather prominent blood supply, giving an idea of the extensive edema present in this lobe.

A slide from another patient who was treated five years earlier and was referred for additional treatment because of recurrent symptoms indicates, I am sure you will all agree, an extreme degree of superficial atrophy, probably with deep atrophy, rather than tumor. In view of what has been seen this morning, I think that the physicist should approach this case with a view to determining how uniform the original dose was and how adequate the tumor dose was before even suggesting or permitting calculations for additional therapy. The deep complications are probably those of atrophy.

In closing, I would like to commend Drs. Arnold and Bailey for this exhaustive type of analysis and to urge that they be given all possible support and encouragement in their current studies on the nervous systems of animals and man.

**K. E. Corrigan, Ph.D.** (Detroit, Mich.): There is nothing in the world quite so satisfying as to see complete confirmation of something that one has presented and which at the time of presentation was the source of controversy. We did practically the same thing as has been reported here and produced almost identical slides twelve years ago, receiving the first prize for our exhibit at the 1940 meeting of this Society.

Our beam sizes were very much more precise than those that have been shown. We used 5.0-mm. beams. The slides that we exhibited at that time showed the precise cut-off effect in the myelin sheath, and we demonstrated beyond any possible doubt that this was a direct effect on the myelin and not an effect on the blood vessels.

We were able to show, also, with a very carefully aimed beam on the dog's complex sensory motor cortex, after the proper spot had been determined experimentally, a whole series of phenomena which could be followed for a period of fourteen months, involving loss of the cortical reflexes, and finally, by sacrificing dogs at intervals from twenty-four hours to fourteen months over a period of four years, we were able to demonstrate all of the details of the early and late changes.

In any case, I thank Dr. Arnold and his group very much for their beautiful confirmation.

**Dr. Arnold (closing):** Since Dr. Corrigan's studies on the central nervous system of the dog were never published, I am unable to comment upon them. Some of his remarks, however, have reference to an excellent paper by Reynolds, that appeared in the *American Journal of Roentgenology and Radium Therapy* in 1946, in which it was demonstrated that the polarizing microscope can be used to show changes in the white matter which previous investigators were able to demonstrate by neurohistological preparations. However, the basic problem as to whether such changes in the white matter are or are not secondary to vascular damage was not answered in this paper. We believe that our preparations do demonstrate that the white matter can be destroyed without the appearance of vascular impairment to account for the extensive selective changes which we are observing in the brain both of the monkey and man, following irradiation with 23-mev x-rays.

In addition, we have been able to outline the histologic and neurologic changes as related to specific tissue doses and to specific time intervals after irradiation. By the use of 23-mev x-rays, employing the beam in the manner which we have

<sup>1</sup> Slides were shown at this point.

described, we can show that there are bilateral areas of comparable radioresponsiveness in the central nervous system of the monkey. This, of course, cannot be demonstrated with use of a source of low-energy x-rays (250 kv.).

Finally, I would be very cautious about interpreting changes in the central nervous system of

dogs, rabbits, and cats, because these animals frequently display extensive cerebral pathology due to an innate encephalomyelitis of virus origin, probably the distemper virus, which will interfere with the interpretation of radiation effects. The monkey, fortunately, is rarely troubled with such encephalomyelitides.



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## Myositis Ossificans Progressiva<sup>1</sup>

EDWARD B. SINGLETON, M.D., and JOHN F. HOLT, M.D.<sup>2</sup>

IN 1692 PATIN (1) described the first case of progressive muscle ossification and in 1868 von Dusch (2) gave the disease its present name of myositis ossificans progressiva. A detailed survey of the literature was published by Rosenstirn (3) in 1918, and in 1932 Mair (4) reviewed the subject thoroughly and published two cases of his own. In Mair's report the suggestion was made that the name be changed to "fibrositis ossificans progressiva" because actually the disease involves the connective tissue rather than the muscles. Although this term is more descriptive of the pathological process, the original nomenclature has common usage and will be employed in this paper. Numerous case reports of myositis ossificans progressiva have appeared in the medical literature in the past half century, and yet it remains a medical enigma.

Antecedent infection, especially rheumatic fever, has frequently been associated with this disease but there is no proof that the relationship is anything but coincidental. Trauma, although definitely responsible for localized isolated areas of ossified muscle, has not been definitely established as an etiological factor in the progressive type of myositis ossificans.

The occasional occurrence of the disease in the same family and the relatively frequent occurrence of the same associated developmental osseous defects in members of the same genetic linkage suggest a familial predisposition. The observation of progressive myositis ossificans in homozygotic twins as reported by Vastine (5) adds substantiating evidence that heredity is influential in the etiology.

The clinical features are frequently characteristic. The disease makes its appearance in infancy or early childhood in

the form of solitary or multiple soft-tissue masses located, as a rule, on the dorsum of the neck or back. The initial soft-tissue lesions may be firm or soft in consistency and occasionally have a tendency to ulcerate the overlying skin (6). These lesions are frequently painful and may be accompanied by local inflammatory changes. After variable periods, from a few days to several weeks, the inflammatory masses may either regress and disappear or become ossified. Frequently during the course of the illness these soft-tissue tumors shrink suddenly in size, and remission of the entire disease may appear to occur. This change has at times been erroneously attributed to various types of treatment, whereas actually it is characteristic of the disease. Gradually the necrotic reaction and resulting ossification spread to involve the connective tissue both in the intermuscular septa and in fascial planes and tendons until complete immobility of the trunk and upper extremities has occurred. Low-grade fever may occasionally be present during the acute phase of the disease, but this is by no means a constant finding.

Congenital osseous anomalies are present almost invariably, the great toes being most frequently involved. Microdactylia of the great toe with ankylosis of the interphalangeal joint and ankylosis of the metatarsophalangeal joint with absence of one phalanx are anomalies commonly encountered. Hallux valgus is also a frequent finding. The first metacarpals may be hypoplastic, as well as many of the phalanges. Some cases have also shown hypoplasia of the middle phalanges of the fifth digits of the hands.

There seems to be disagreement as to the histologic picture in the acute phase of the

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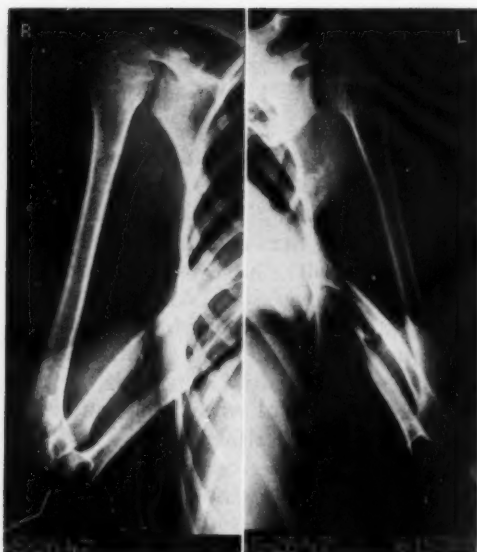


Fig. 1. May 26, 1947. Although only faint areas of calcification are seen within each axilla, the degree of immobility of both arms and the flexion deformity of the forearms was nearly as severe as on the more recent admission of Aug. 21, 1952.

evidenced by roentgenograms made at the onset of the disease as well as later, after muscle ossification had occurred. In addition, the case offers certain other unusual features which perhaps justify its introduction into the medical literature.



Fig. 2. The first metacarpal of each hand is abnormally short. The second phalanx of each fifth digit is also slightly shorter than normal.

process. According to Geschickter (7) the earliest histologic findings consist of degeneration and necrosis of the muscles and hyperplasia of the surrounding connective tissue. Inflammatory cells accompany the degenerative process. Islands of osteoid tissue spring up and become invaded by osteoblasts; cartilage may also be formed. Most pathologists now believe that the muscles are involved secondarily by the initial process which affects the connective tissue of the fascia and tendons as well as the intermuscular fibrous septa, the necrosis of muscle bundles being the result of pressure from the surrounding ossified connecting tissue. In later stages of the disease biopsy specimens show fairly normal bone. Significant abnormality of the blood chemistry has not been demonstrated.

Most of the reported cases show the disease in an advanced form and to our knowledge there are no reports in the English literature of the earlier stages.

The following case demonstrates the progressive nature of the condition as

#### CASE REPORT

*First Admission* (May 21, 1947): A. R., a 9-year-old white boy, entered the University Hospital complaining of rigidity of the back and arms. He had been well until the age of five years, when there developed a "lump on his tailbone." Roentgenograms at that time reportedly showed multiple bony exostoses on the knees, toes, and spine. In January 1947, marked stiffness of the back occurred and on March 10 a non-tender tumefaction was noticed over the posterior portion of the left shoulder. Biopsy of this area was reported as "negative." Hot compresses were applied to the mass and penicillin was administered intramuscularly. Two weeks later the swelling disappeared but was soon succeeded by a similar mass over the right scapula and by increased thickness of the neck muscles. A week later induration over the left biceps was noted. On April 29, an urticaria-like rash appeared over the entire body.

*Physical Examination:* The patient was undernourished. He sat and walked with his spine fixed and straight. His arms were rigid with the forearms flexed across the lower portion of the thorax. His temperature was 99° F., pulse 86, respirations 15. He weighed 68 lb. and was 56 3/4 inches tall. His head was held in a slightly flexed position, and all movements were markedly restricted. The submaxillary, cervical, and axillary lymph nodes were slightly enlarged. Respiratory movements were diminished. The heart was normal in size, with normal rhythm and rate. No murmurs were heard. A hard mass was palpable over the occiput. The

posterior neck muscles on the right were enlarged. A bony mass measuring 4 cm. in diameter was palpated over the right scapula, and a small bony projection was noted over the coccyx. The boy was unable to move his forearms from their flexed position, and shoulder movements were markedly limited. The fingers and wrists were not involved.



Fig. 3. Bilateral hallux valgus deformity is present and the proximal phalanx of each great toe is abnormally short. These findings, suggestive of localized chondrodysplasia, are frequently observed in patients with myositis ossificans progressiva.

nor was there limitation of movement of the lower extremities. A hard mass, 6 inches in length, was palpable in the right biceps muscle and a smaller mass could be felt in the left biceps. The great toes were small, and bilateral hallux valgus deformities were present. The skin showed a generalized maculo-papular rash which was diagnosed as scabies and treated successfully.

**Laboratory Findings:** The hemoglobin was 15 gm.; red blood cells, 4,720,000; white cells, 8,100, with a normal differential. Urinalysis was negative. The Kahn test was 2+ on the initial examination but was negative on attempted verification test. The tuberculin test was negative at a dilution of 1:1,000. Total blood protein was 6.6 gm. per 100 c.c.; albumin 4.1 gm. per 100 c.c.; globulin 2.1 gm. per 100 c.c. Acid base studies showed the  $\text{HCO}_3$  to be 25.1 milliequivalents per liter. The blood urea nitrogen was 12.7 mg. per 100 c.c. Urinary calcium excretion at the forty-eighth hour, on a diet free of milk and cream, was the same as on a controlled urine. From May 24 to July 6 eight studies were made to determine the serum level of calcium, phosphorus, and phosphatase. The serum calcium ran from a high of 11.3 mg. per cent to a low of 5.7 mg. per cent; phosphorus from a high of 6.3 mg. per cent to a low of 4.8 mg. per cent; phosphatases from a high of 7.9 Bodansky units to a low of 4.7 Bodansky units. (These fluctuations were considered to be inaccuracies on the part of the laboratory.)

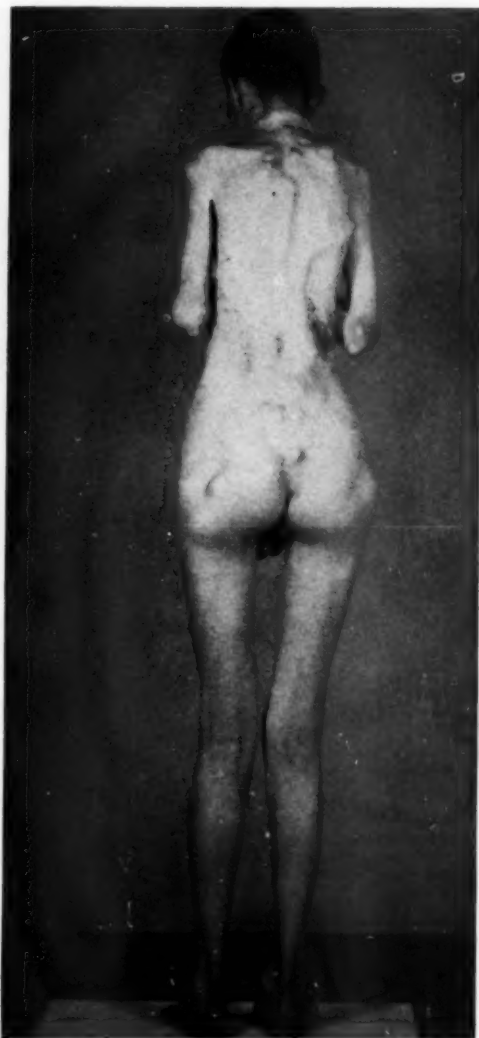


Fig. 4. The patient at the time of the second admission on Aug. 20, 1952. The osseous "lumps" are obvious. The ridge of bone in the right paraspinal muscles with extension into the right latissimus dorsi is clearly seen.

**Roentgen Findings (June 1, 1947):** Films of the cervical spine showed partial fusion between the lamina of C-4 and C-5 and apparently complete osseous fusion between the articulating processes and lamina of C-5 and C-6, and C-6 and C-7. The corresponding vertebral bodies were reduced in size, especially in their anteroposterior diameters. The thoracic and lumbar portions of the spine were normal in appearance. A small bony prominence was present over the posterior portion of the lower sacrum. This was thought to represent a small

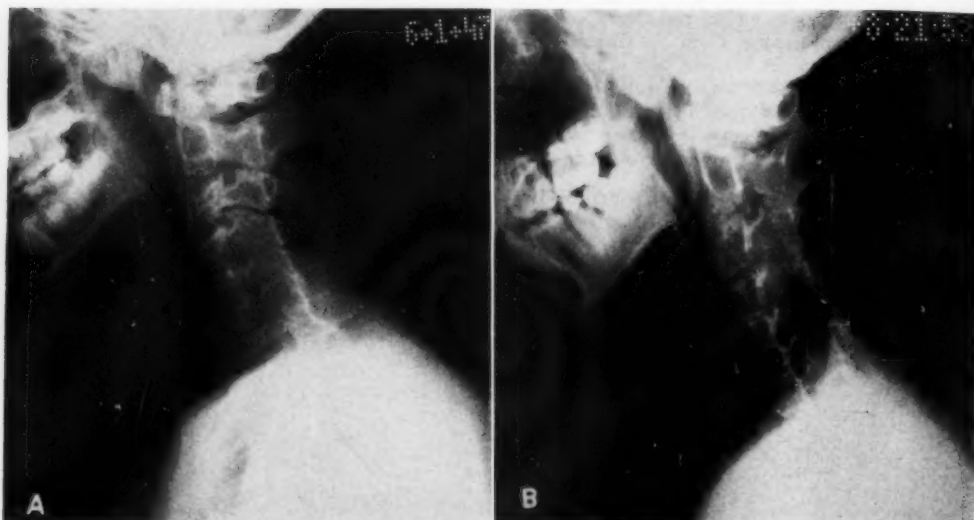


Fig. 5. A. Anomalous development of the cervical spine with small cervical vertebrae and fusion of the lamina in the lower portion, as seen in 1947. B. Progression of the process with obliteration of several of the intervertebral foramina, five years later.



Fig. 6. The bony bridge (arrow) extending from the superior border of the left scapula into the left side of the neck is believed to be in the trapezius muscle.

exostosis. Chest films showed ill-defined areas of calcification in each axilla (Fig. 1) with extension to the posterior chest wall on the right and onto the anterior chest wall on the left. A small similar area of calcification was seen in soft tissues at the base of the neck on the left.

Films of the upper extremities showed multiple

cartilaginous exostoses involving the distal portion of the left radius, the distal portion of the left femoral metaphysis, the proximal tibial metaphysis, and the distal diaphysis of the right fibula. Films of the hands showed that the first metacarpal was abnormally short bilaterally. In addition, there was shortening of the middle phalanx of each fifth finger (Fig. 2).

Films of the feet showed bilateral hallux valgus deformities with shortening of the proximal phalanx of each great toe (Fig. 3).

*Hospital Course:* During this admission the patient was afebrile and was comfortable until the thirty-fourth hospital day, when he complained of interphalangeal swelling of both hands. He experienced little benefit from physiotherapy and was discharged without significant improvement.

*Second Admission* (Aug. 20, 1952): The patient, now fourteen years old (Fig. 4), was referred from the Michigan Crippled Children's Commission for the possibility of improvement of shoulder function and for surgical removal of some of the irritating exostoses. There had been little change in the degree of his disability since the previous admission and, except for the immobility of his spinal column and upper extremities, he was asymptomatic.

*Past History:* The patient stated that he had measles early in childhood. He gave no history of allergy, pulmonary disease, or rheumatic fever. He reported that one of his legs was fractured when he was two years old but he could not recall which extremity was involved. For the past two or three years he had noticed moderate exertional dyspnea.

*Family History:* The patient's mother and father





Fig. 7. A. The normal appearance of the spinal column in 1947. B. In 1952 extensive bone formation has occurred within the right posterior spinal muscle bundles. Similar but less extensive bone formation has occurred on the left side of the spine. Note also the bone formation posterior to the left hip joint.

and four grandparents were living and well at the time of this admission. He had a brother and sister who were also well. There was no history of osseous anomalies in the family, nor had there been diseases similar to that of the patient.

**Physical Examination:** The same degree of deformity was present as on the first examination. The face was mask-like. The temperature was 99.4° F., pulse 90, respirations 20, and blood pressure 100/68. The patient was 5 ft. 8 inches tall, poorly developed, and undernourished. Large dome-shaped masses were visible over the posterior scapular areas, and a ridge of bone was present over the left posterior chest, extending from the angle of the left scapula medially and inferiorly into the lumbar area, where several raised areas of bony hardness were present. The neck, entire spinal column, and both shoulders were immobile, and the forearms were crossed over the lower portion of the

chest and fixed in position. Multiple exostoses were palpable over the sternum and ribs. A bony mass was palpable in the right rectus femoris muscle, extending from the region of the anterior superior iliac spine to the midportion of the right femur.

**Roentgen Findings:** Films of the cervical spine showed bony bridging between the articulating processes and laminae between C-3 and C-7, with obscuration of the intervertebral foramina between C-3 and C-4, C-4 and C-5, and C-5 and C-6 (Fig. 5). A bony bridge extended from the superior angle of the left scapula upward to the midcervical region (Fig. 6). In the dorsal spine, bone formation was demonstrated paralleling the spinous processes, producing solid bony union between the dorsal vertebrae. Films of the lumbar spine showed a sheet of bone extending from the sacrum superiorly along the right side of the vertebral bodies into the

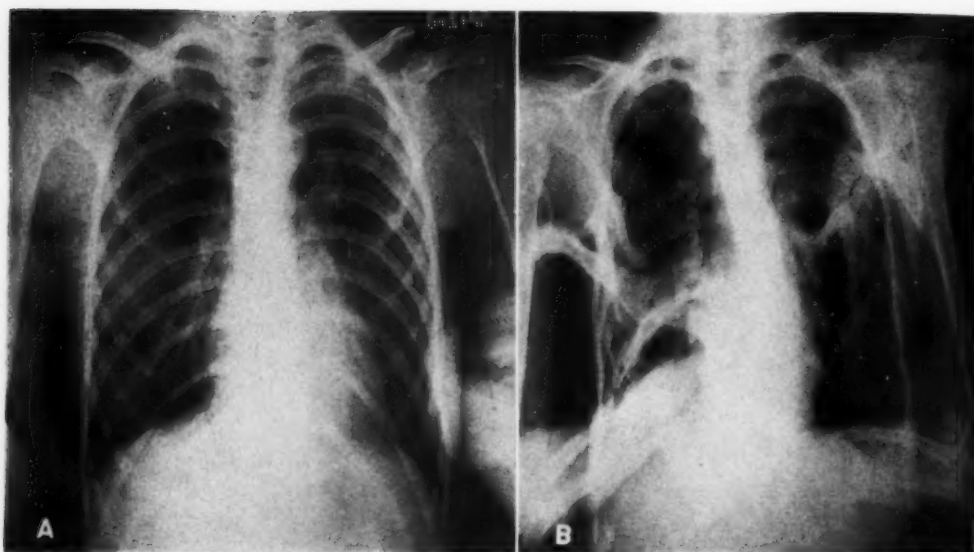


Fig. 8. A. Calcification within soft tissues of each axilla was faintly visualized at the time of the first hospital admission. B. Five years later extensive bone formation has occurred. The degree of immobility of the arms was essentially the same on both dates.



Fig. 9. The superior portion of the right humerus is irregularly mineralized, and its appearance suggests faulty conversion of cartilage to bone.

lower dorsal area. Similar but less extensive calcification was noted on the left side of the upper lumbar vertebrae (Fig. 7).

Chest films showed bone formation extending

from the posterior chest wall in the right paraspinal region to the medial side of the proximal portion of the right humerus (Fig. 8). This was thought to lie in the latissimus dorsi muscle. Smaller bony bridges were present in the same region in the right axilla. The anterior portions of the right third and fourth ribs were thickened and had a wavy contour. A synostosis between the posterior portions of the right ninth and tenth ribs was noted. There was ectopic bone formation on the left anterior chest wall extending across the anterior portion of the left axilla to enter the upper half of the left humerus. This area of abnormal bone was believed to lie in the pectoralis major muscle. Additional but less extensive bone formation was present on the posterior chest wall, connecting the vertebral border of the left scapula with the spinal column. A small exostosis projected from the superior portion of the right sixth rib.

Films of the right shoulder showed irregular trabeculation and multiple lytic areas separated by bony septa involving both the epiphysis and metaphysis of the right humerus (Fig. 9). Irregular trabeculation was also apparent in the left shoulder, but the degree of this malformation was not so severe as on the right side. A single exostosis projected medially from the diaphysis of each humerus.

Films of the forearms revealed flexion deformities at the elbow joints. A sharp exostosis projected proximally from the midportion of the shaft of the left ulna. Slight bowing of each radius was present.

In the left femur a slender exostosis was demon-

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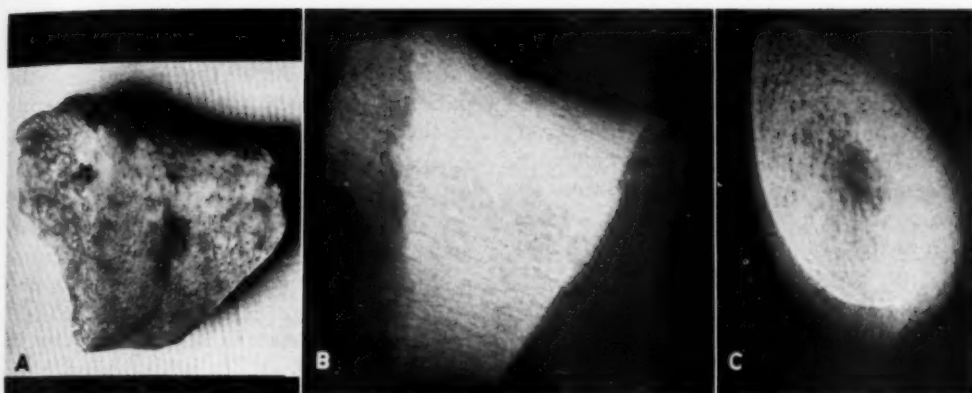


Fig. 10. A. Segment of bone removed from left pectoralis major muscle. B and C. Roentgenograms of specimen showing trabecular bone and marrow cavity.

strated, extending superiorly from the medial side of the distal metaphysis. The right femur showed calcification in muscle in the region of the proximal portion of the rectus femoris.

Films of the lower legs revealed cartilaginous exostoses located about the proximal metaphyses of both right and left tibiae. There was some broadening of the proximal metaphysis of each tibia due to lack of molding of this portion of the bone. In the pelvis there was bone formation in the region of the left gluteal muscle extending posteriorly to the neck of the left femur. Minimal coxa valga deformity was present, and there was some broadening of each femoral head.

**Laboratory Studies:** The serum calcium was 11.4 mg. per 100 c.c.; phosphorus 4.8 mg. per 100 c.c., alkaline phosphatase 15.5 King-Armstrong units.

**Hospital Course:** Two weeks after admission, a segment of bone was removed from the left pectoralis major muscle (Fig. 10). The ends of the remaining segments of bone were painted with formalin as a prophylactic measure against bone regeneration in this area. The patient was discharged several weeks later without significant improvement.

**Pathological Report:** After decalcification, the specimen consisted of cancellous bone containing heavy trabeculae. Fatty bone marrow was present. Muscle structures were not identified in the specimen.

#### DISCUSSION

It is interesting that at the time of the patient's first admission only a small amount of soft-tissue calcification could be seen in each axilla and at the base of the left side of the neck, and yet the degree of disability was approximately the same as on the last admission, at which time

extensive ectopic bone formation was readily detectable. This suggests that the replacement of the degenerating connective tissue in the fascia, tendons, and intermuscular septa by extensive fibrosis accounts for the immobility rather than the ossification of these areas which occurs later in the course of the disease. This in turn raises the question as to whether adrenocorticotrophic hormone or cortisone may not be beneficial in the early stages of the process.

Although the changes in the cervical spine described during the first admission strongly suggested a variation of the Klippel-Feil type of deformity, the films obtained on the second admission showed an increase in the degree of fusion between the lateral masses, thereby indicating that the original changes represented bone formation in intervertebral fascia rather than congenital failure of segmentation.

The deformities of the feet seem to be invariably associated with this disease; anomalies of the hands, although less frequently present, are often encountered.

The changes in the proximal portion of the right humerus have more the appearance of an enchondroma than of the osteoporosis of disuse, although this has not been proved. However, in view of the fairly frequent association of multiple exostoses with myositis ossificans pro-

gressiva, it seems logical to assume that enchondromata may also be formed. This further suggests that the basic abnormality lies in the primitive mesenchymal tissue. The frequent association of a wide variety of apparently unrelated osseous congenital abnormalities further substantiates this assumption.

Immediately after resection of the segment of bone in the left pectoralis major muscle, the patient was able to abduct the left arm slightly. At the time of discharge, however, there was clinical evidence that re-ossification was occurring in the resected area. This confirms other reports that surgical intervention is not beneficial.

#### SUMMARY

A case of myositis ossificans progressiva with certain unusual features is presented in this report. Roentgenograms made during the onset of the disease as well as later in the course of the patient's illness

show graphically the progressive nature of the condition.

Strangely enough the extent of the patient's disability changed little in spite of the extensive roentgenological changes.

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#### SUMARIO

##### Miositis Osificante Progresiva

Preséntase un caso de miositis osificante progresiva, en el cual se obtuvieron radiografías al iniciarse la enfermedad así como cinco años más tarde, después de haber osificación muscular. Las mismas revelan claramente la naturaleza evolutiva de las alteraciones.

El enfermo fué observado por primera vez a la edad de nueve años, con rigidez del dorso y de los brazos. Roentgenológicamente, no podía observarse más que cierta pequeña proporción de calcifica-

ción en cada axila y en la base del lado izquierdo del cuello; sin embargo, la incapacidad era aproximadamente idéntica que cinco años después, cuando ya podía distinguirse fácilmente extensa osteogenia ectópica. Esto indica que la inmovilidad que caracteriza a la afección procede de la substitución del tejido conjuntivo en vías de degeneración en las aponeurosis, tendones y tabiques intermusculares por fibrosis extensa, más bien que de la osificación más tarda de dichas zonas.



## Fungous Infection of Bone<sup>1</sup>

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THE BACTERIOLOGIC and roentgenologic aspects of fungous disease of bone are well known to the many physicians interested in mycotic infections. The criteria for the roentgen diagnosis have been described and effectively correlated with the pathological observations. Often, however, in spite of all the information available, those who are called upon to give opinions on cases of fungous disease find it impossible to offer a definite interpretation or are even led into making a wrong diagnosis. It is for this reason that a review of the subject seems timely.

So much has been written on the various phases of fungous infection and the morphological and cultural characteristics of the various organisms that a further account is not necessary here. Figure 1 will serve as a general description.

In our series of 40 cases of fungous disease of bone, blastomycosis predominated, accounting for 23; actinomycosis accounted for 16, and cryptococcosis for 1. Luck (4), on the other hand, has found blastomycosis of much less common occurrence than either actinomycosis or coccidioidosis.

### BLASTOMYCOSIS

Blastomycosis occurs in two forms, cutaneous and systemic. In a series of 47 cases, we found the lungs involved in 84 per cent, the skin in 89 per cent, and the bones in 47 per cent. Skeletal involvement may be either by direct extension or by hematogenous spread from an unknown portal of entry.

In the long bones there is a tendency for the infection to lodge in the epiphyses. Extension by rupture of an epiphyseal abscess is responsible for most of the joint

lesions (5). Only 1 of our patients gave a history of a minor injury to the affected part preceding the onset of symptoms.

The bone and joint lesions of blastomycosis simulate very closely those of coccidioidosis (6). Involvement of the spine may resemble Pott's disease, except that the process is usually more extensive than in the latter condition. Several vertebrae and ribs may be involved simultaneously. Of the long bones, those of the lower extremities are chiefly affected. The disease may remain confined to a single bone or may extend into and beyond the joint, as in the short bones.

The radiographic findings are variable. A consistent feature is a sharp line of demarcation between the area of involvement and the adjacent normal bone. Many years ago, Dr. Hollis Potter wrote: "The bone surrounding the blastomycotic focus presents a normal structure with little tendency to change in density."

The prognosis of osseous blastomycosis is variable. Death may occur in six to eight months. On the other hand, survivals of five, eleven, and thirteen years have been reported. Better results may be obtained with the more careful use of stilbamidine. It seems, however, that visceral lesions respond more readily than those of osseous origin.

CASE I (Fig. 2): A 28-year-old farmer was seen in 1940, giving a history of a mass in the left epitrochlear region of a year duration. The mass was incised and drained for eleven months. During this time the patient began to experience pain and stiffness in the back. A roentgenogram showed questionable paravertebral infection and involvement of the 8th dorsal vertebra. Aspiration biopsy disclosed blastomycosis. Treatment was started with small doses of iodides, carried to tolerance. This was continued for three

<sup>1</sup> From the Department of Radiology, Duke University, Durham, N. C. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

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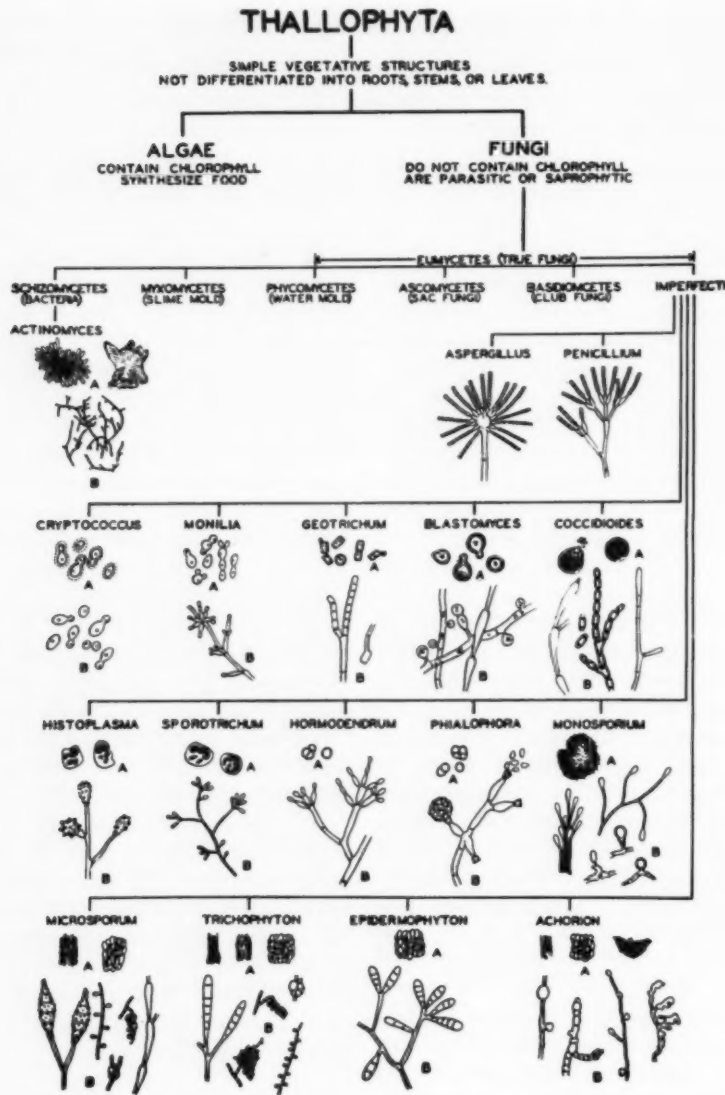


Figure 1

months, followed by a rest of three months. In the meantime, the spine was placed in a metal brace. The infection eventually cleared, and follow-up films showed gradual healing. Examination in June 1952, showed the process arrested.

#### ACTINOMYCOSIS

Actinomycosis is a chronic infective granuloma found most frequently in Mississippi, North Carolina, and the northwest-

tern states. More than half of the lesions occur in the head and neck. Six of our 16 cases were primary in the jaw. Bone involvement is almost invariably by direct extension from adjacent soft tissues. Very rarely a primary lesion arises in a bone.

The dorsal vertebrae are usually involved by extension from the lungs, and the lumbar vertebrae by extension from

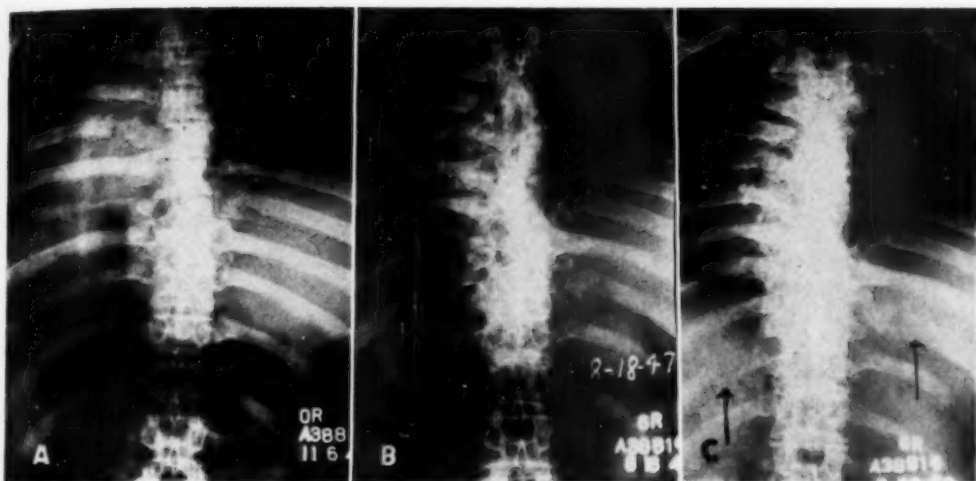


Fig. 2. Case I. Blastomycosis of the spine, showing extensive osteomyelitis and paravertebral abscess, with healing over a ten-year period. A. On admission, in 1940. B. Aug. 18, 1947. C. June 30, 1950.



Fig. 3. Case II. Bone destruction in the mandible, due to actinomycosis.

the abdominal viscera. When the disease infiltrates the lungs, involvement of the ribs, sternum, and vertebrae usually suggests actinomycosis rather than anything else. The roentgen appearance is that of a granulomatous destructive process. In the spine there is erosion of all portions of the vertebrae, including the pedicles and laminae, and frequently the process extends to the adjacent ribs. Collapse of a vertebra is comparatively rare. The intervertebral disk is usually intact.

CASE II. A 54-year-old Negro farmer noticed

swelling of the jaw two weeks after tooth extraction. Laboratory culture showed *Actinomyces bovis*. A direct smear was also positive. A roentgenogram of the mandible showed an area of bone destruction. Following surgical drainage, x-ray therapy, and administration of penicillin and sulfa drugs, the patient gradually improved and the sinuses closed (Fig. 3).

#### CRYPTOCOCCOSIS

Cryptococcosis is widely known as torulosis and sometimes as European blastomycosis. The causative organism, *Cryptococcus neoformans* or *Torula histolytica*, like *Blastomyces* and *Actinomyces*, is one



Fig. 4. Case III. *Cryptococcus* infection of the carpal bones (A) and similar osteolytic lesions in the foot (B). The follow-up films (C and D) obtained two years later show a considerable degree of healing.

of the *Fungi imperfecti*. It has frequently been mistaken for a lymphocyte or red blood cell. The gelatinous or mucoid character of the exudate often gives the impression of myxomatous tumor tissue. The bone lesions are quite similar to those of blastomycosis and coccidioidomycosis (7). These three mycoses differ from actinomycosis both in the distribution and the character of the osseous lesions. The histopathologic characteristics of cryptococcosis have been said sometimes to re-

semble those of Hodgkin's disease and sarcoïd.

Roentgenograms disclose widely disseminated and discrete lesions, which tend to be purely destructive, with little or no reaction in the bone or periosteum but surrounded by a well marked proliferation of bone. There seems to be a slow rate of change in the disseminated areas of destruction.

Our single case of cryptococcosis follows:

CASE III: C. W., a white farmer, had a pharyngeal and tonsillar lesion of four months



duration, as well as an infection over the left side of the nose. The physical examination disclosed, also, a slight swelling of the left ankle, thought to be due to recent trauma, and moderate pain in the right wrist. Smear and culture showed *Cryptococcus*. Roentgenograms demonstrated osteolytic lesions of the carpal bones and the bones of the foot (Fig. 4). The patient was treated with Propamidine, intramuscularly, 39 mg. daily for two days, followed by 78 mg. for two days, then 117 mg. for two days, and finally by 156 mg. for two days. This course was repeated twice at two-week intervals, with notable improvement in the patient's condition, clearing of the lesions, and filling in of bone.

#### COCCIDIOIDAL GRANULOMA

Coccidioidal granuloma of bone usually starts as a purely destructive process in the spongiosa. The margins of the area of decreased density may be sharply circumscribed or poorly defined. New bone formation and periosteal proliferation are unusual but may occur as a late change. In some instances the first area of destruction is in the cortex of the bone adjacent to an abscess in the soft tissues. Both the epiphyses and diaphyses may be involved and there may be direct extension to the joint. In numerous cases there is a visible soft-tissue mass around the area of diseased bone. The bones most commonly affected are the ribs and lower ends of the tibiae and fibulae, though Carter (6) has described lesions in the clavicle, scapula, humerus, ulna, radius, femur, fibula, skull, ribs, vertebrae, pelvis, hands, and feet. In other words, there may be diffuse osseous involvement.

The roentgen appearance is not characteristic and may be confused with tuberculosis, syphilis, osteomyelitis, actinomycosis, blastomycosis, and metastatic cancer. The diagnosis may be suspected in the presence of skin manifestations, adenopathy, and pulmonary lesions. Joints are rarely involved, except by direct extension from neighboring structures.

#### SPOROTRICHOSIS

Sporotrichosis is a granulomatous disease usually confined to cutaneous or subcutane-

ous structures but it may involve viscera and bony structures. The course is usually that taken by other granulomata of mycotic origin. Osseous involvement may include the joints, articular surfaces, and synovial membrane. Bone lesions are almost always accompanied by skin lesions. The changes in the phalanges are similar to those seen in syphilitic and tuberculous dactylitis. While the infection may last for several years, it rarely is fatal.

#### DISCUSSION

Fungous infection is widespread, manifesting itself in many forms. More than half the population have some form of dermatosis. The bones may be involved either primarily or secondarily. At the onset the disease resembles acute osteomyelitis; in its advanced stages it may be confused with chronic osteomyelitis and tuberculosis. There are certain findings, however, that are not observed in osteomyelitis and tuberculosis. One of the most consistent is a mild febrile reaction, with absence of leukocytes. Persistent sinus tracts may develop, in which the fungi are often found on direct smear.

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(Para el sumario en español véase la página siguiente.)

## SUMARIO

## Micosis Oseas

En una serie de 40 casos de micosis de los huesos, correspondieron 23 a la blastomicosis, 16 a la actinomicosis y 1 a la criptococosis.

El aspecto radiográfico de las lesiones óseas de la blastomicosis varía. Una característica constante es una línea neta de demarcación entre la zona atacada y el hueso normal adyacente. Las lesiones actinomicóticas de los huesos toman roent-

genológicamente la forma de procesos granulomatosos destructores. En la criptococosis, la invasión ósea está muy diseminada y es discreta, siendo las lesiones casi absolutamente destructoras, y estando rodeadas de una proliferación bien definida de hueso nuevo.

Preséntanse casos típicos de dichas dolencias, discutiéndose sucintamente otras micosis que afectan el hueso.

## DISCUSSION

**L. Henry Garland, M.D.** (San Francisco, Calif.):<sup>1</sup> Dr. Reeves has presented a timely and concise review of the roentgen findings in fungous infection of bone. As he correctly points out, this group of diseases is one in which personal examination of the patient by the radiologist at the time of roentgen examination often gives a useful clue to the correct diagnosis. In these days of large volume of x-ray work in busy offices and departments, personal interviews prior to x-ray examination are made all too seldom. In many smaller units such personal examination is customary, giving perhaps a greater opportunity for early x-ray diagnosis of these lesions.

The soft-tissue mass over the chest in a patient with x-ray evidence of chronic rib disease, the swollen tongue or submandibular structures in a patient with osteomyelitis of the mandible, and the draining sinus about the ankle in a patient with chronic infection of the fibula, are all useful clues. Nevertheless, even in the presence of such soft-tissue changes, microscopic examination of the discharge or the tissues is essential for completion of diagnosis. The point regarding sharp demarcation between normal and involved bone in blastomycosis is one that is seldom mentioned and is apparently a useful differential clue. In bone lesions due to coccidioidomycosis, the involvement is usually multiple, and the points of predilection are the bony prominences (a feature sometimes of use in differentiating these lesions from those due to tuberculosis). The lesions in coccidioidomycosis are usually destructive, but when secondary infection occurs, variable degrees of bone or periosteal change may be present to mask the underlying destruction.

It is of interest to note that a majority of the cases reported by Dr. Reeves were blastomycosis. This reminds us of the predominantly regional pattern of fungous diseases. The lesions which he would call blastomycosis in North Carolina we would tend to call coccidioidomycosis in

California, and each of us would be right most of the time in our respective geographic locations. That is, as long as tuberculosis could be excluded! We have seen only one case of torulosis of bone and no proved cases of sporotrichosis; judging from the literature and from the report of Dr. Reeves, there are no characteristic findings in these diseases either.

We have had the same experience as the speaker in connection with actinomycosis of the spine, namely, that involvement of the intervertebral disks is exceptional. I would like to ask Dr. Reeves one question: In how many of his cases of osseous blastomycosis was there concomitant pulmonary blastomycosis?

**Sydney F. Thomas, M.D.** (Palo Alto, Calif.): There is a question I would like to ask Dr. Reeves: Is there an acute component to blastomycosis as there is in coccidioidomycosis?

**Dr. Reeves (closing):** I think the assumption is quite correct that in one part of the country blastomycosis might be more common, and in another—California—coccidioidomycosis would predominate. Though I did not mention this, the skin tests are frequently interchangeable. I have seen this happen several times. Even though *Blastomyces* was demonstrated by the mycologist, the patient was sensitive to the coccidioidin vaccine. This brings in the mycologist, who is very important in this study, to identify the organisms.

Sixty-eight per cent of the patients with osseous blastomycosis had pulmonary infection. In fact, we find this association quite common. Frequently the lesions in the lung were found first, the patient having been referred on that account.

We have seen a few cases of acute blastomycosis. One Negro patient died with very acute widespread systemic disease, with skin lesions and later pulmonary involvement, but without bone lesions.

<sup>1</sup> Read by Dr. Sydney F. Thomas.

## Radiological Evidence of Growth in Children with Acute Leukemia Treated with Folic Acid Antagonists<sup>1</sup>

HARRY A. WAISMAN, PH.D., M.D.,<sup>2</sup> and ROGER A. HARVEY, M.D.

THE ABILITY OF folic acid antagonists to provide temporary bone marrow remissions in children with acute leukemia has been described by many investigators since the initial account by Farber and his co-workers (2). A clinical report from this laboratory by Poncher *et al.* (4) provided corroborative evidence that antagonists were able to prolong life and that temporary bone marrow remissions were accompanied by definite improvement in the osseous manifestations of the disease. The average duration of life in untreated acute leukemia patients was five and a half months and in the folic acid antagonist-treated group thirteen and a half months. This prolongation of life was shown to be statistically significant. Since the growth process appeared to be uninterrupted in spite of the long duration of the disease (more than two years in several cases), it seemed of interest to evaluate radiographic findings in 21 patients treated prior to the antagonist era, and in 43 patients to whom antagonists were administered, at this institution.

Roentgen manifestations of leukemic infiltration and proliferation in the skeletal system are fairly well known and frequently are specific enough to warrant a presumptive diagnosis, although it is usually a late diagnosis. Changes are most frequently encountered in children, where bone growth is rapid and the disease takes a more uniformly acute or subacute course than in adults. The bone changes can usually be classified into several categories, and one or more manifestations may be present at the same time. These categories are:

1. Localized or disseminated areas of diminished density.

2. Periosteal elevation with subperiosteal new bone formation.

3. Narrow zones of decreased density near the ends of long bones.

4. Localized or scattered areas of increased density, usually occurring late in the disease, possibly manifestations of attempted repair.

5. Transverse lines of increased density near ends of long bones.

Other changes also occur, but are most often associated with unusual types of leukemia.

Several reports in 1950 indicated that the folic acid antagonists brought about definite resolution or arrest of leukemic bone manifestations. Silverman (5) described 8 cases and observed transverse bands of diminished density near the ends of long bones, with eventual appearance of demarcating lines of slight increase in density. These roentgen changes were not considered specific in nature but were regarded as evidence of temporary arrest of the disease as a result of the treatment, especially since their appearance generally coincided with clinical and hematological evidences of remission. Dresner (1) reported disappearance of radiographic evidence of the disease following antagonist therapy, but stressed that this did not imply complete healing and that there was little relationship to leukemic infiltration elsewhere in the body. Karpinski and Martin (3) also observed resolution of skeletal lesions with this therapy.

A review of our cases not treated with antagonists showed no uniform tendency to form transverse zones of diminished or increased density. However, the antagonist-treated group frequently showed transverse phenomena and, in the patients whose lives were extended by this treatment, the zones became quite characteristic of local arrest of the disease process,

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<sup>2</sup> Now in the Department of Pediatrics of the University of Wisconsin College of Medicine, Madison, Wis.

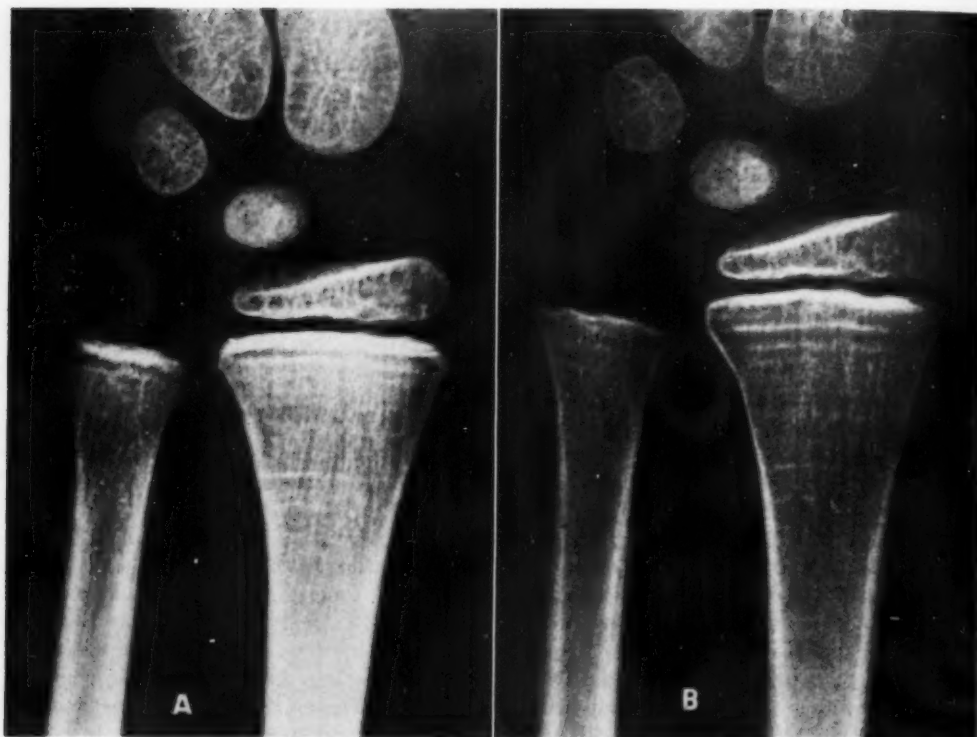


Fig. 1. A. Transverse bands of decreased density near ends of long bones in a 6-year-old boy (J. B.) with acute stem-cell leukemia identified three months earlier. Treated with antagonist. B. Same patient seven months later. Continued bone growth is obvious by new location of band.

and bone growth continued at an apparently normal rate in spite of recurring exacerbations and remissions of the primary disease.

Figure 1A shows the slightly demineralized zone with sharp marginal demarcation near the end of the long bones in a six-year-old boy with acute stem-cell leukemia treated with the folic acid antagonist Aminopterin. His disease was identified three months prior to obtaining this film. Figure 1B, from the same case seven months later, shows the banded zone definitely incorporated in the shaft as a result of continued growth of the bones. Figure 2A is from another patient, two years of age, with acute stem-cell leukemia. The changes here are more in the form of dense transverse zones near the ends of the bones. Figure 2B, eleven and a half months later, shows the character-

istic band of decreased density having been carried well up in the shaft as bone growth apparently continued during repeated courses of Aminopterin therapy. Figure 3 is a final film on a four-year-old boy with acute lymphatic leukemia. The extensive zone of altered density and pattern coincides roughly with a four-month exacerbation of the disease thirty months previously. This example is the most striking from our series of antagonist-treated patients and is important from the standpoint of demonstrating continued growth of bone during periods of remission and relapse, and in spite of the severe manifestation of the disease.

The preceding examples are also of significance in that folic acid antagonists apparently prevented the appearance of new bone lesions except terminally, since most of the cases were undergoing repeated ex-



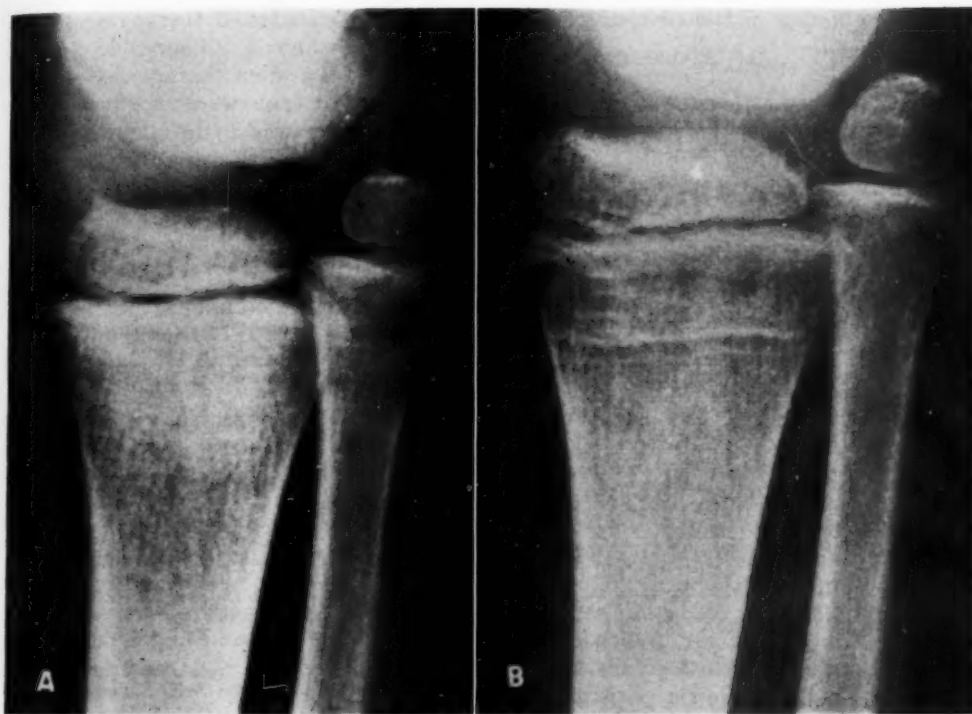


Fig. 2. A. Case of 2-year-old boy (B. M.) with acute stem-cell leukemia with latest flare-up three months earlier. Transverse band is more conspicuously dense in this case. B. Same patient eleven and a half months later. Note decreased density of band and evidence of bone growth in interim.

acerbations and remissions during the period of radiographic observation. Our radiographic material does not lend itself to statistical summaries, since many of the patients did not have periodic radiographic surveys, while in others progressive work-ups were done in different institutions at different stages of the disease. Attempts at correlating the radiographic changes with local autopsy findings have been unsuccessful, since autopsy permissions on most of these cases were restrictive. The reports of Silverman (5) and Dresner (1), however, provided pathologic data regarding these transverse bands. They are evidently a result of alterations in trabecular development due to competition for space with infiltrating and proliferating leukemic cells during the periods of active progres-



Fig. 3. Case of 4-year-old boy (T. B.) with acute lymphatic leukemia. Broad transverse band of markedly altered trabecular detail originating thirty months earlier during a four-month flare-up of the disease. →

sion of the disease in the osseous system.

#### SUMMARY

Forty-three pediatric patients with acute leukemia treated with folic acid antagonists showed a definite arrest of the leukemic infiltration of bone. Additional observations included (a) absence of radiographic evidence of subsequent osseous involvement with exacerbations of clinical symptoms, (b) a tendency to the formation of distinct transverse bands, more often of diminished than increased density, and (c) continued growth of bones at an apparently normal rate during prolonged periods of remission. The arrest of further bony involvement in the face of repeated exacerbations of the disease during antagonist therapy is of distinct interest, since the patients had extensive soft-tissue and organ involvement. The illustrations present some of the longest radiographic follow-ups made in connection with acute leukemia.

A group of 21 pediatric patients with acute leukemia treated before the advent

of folic acid antagonist therapy served as controls and showed radiographic changes in the osseous system characteristic of the disease. Most cases were rapidly progressive and there was little opportunity to evaluate bone growth during the course of the disease.

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#### SUMARIO

#### Signos Radiológicos del Desarrollo en Niños con Leucemia Aguda Tratados con Antagonistas del Ácido Fólico

Cuarenta y tres enfermos pediátricos con leucemia aguda tratada con antagonistas del ácido fólico revelaron estacionamiento bien definido de la infiltración leucémica del hueso. Otras observaciones comprendieron: (a) ausencia de signos radiográficos de subsiguiente invasión ósea con exacerbaciones de los síntomas clínicos, (b) tendencia a la formación de bandas transversales bien demarcadas, más a menudo de menor que de mayor densidad, y (c) continuo crecimiento de los huesos a una velocidad aparentemente normal durante períodos prolongados de remisión. El cese de nueva invasión ósea en presencia de repetidas exacerbaciones de la dolencia

durante la terapéutica antagónica posee decidido interés, dado que había en los enfermos extensa invasión de los tejidos blandos y los órganos.

Un grupo de veintiún enfermos pediátricos con leucemia aguda, tratados antes del advenimiento de la terapéutica con antagonistas del ácido fólico sirvió de testigo, revelando alteraciones radiográficas del sistema óseo, típicas de la enfermedad, pero sin tendencia uniforme a la formación de zonas transversales de densidad ya mayor o menor. La mayor parte de estos casos eran de evolución rápida, ofreciendo poca oportunidad para justipreciar la osteogenia durante la marcha de la dolencia.

## Radiation Sickness in the Monkey<sup>1</sup>

EARL ELDRED<sup>2</sup>, M.D., and WILLIAM V. TROWBRIDGE, M.D.

MUCH OF THE animal experimentation in the field of ionizing radiation has been directed toward the solution of practical problems relating to man, either in therapy or nowadays in industry and possibly warfare. In view of this interest, it is surprising that subhuman primates have been used so little as subject animals. A few investigators have worked on portions of the monkey's body (1, 2, 3), but the effects of total-body irradiation seem to have been described only by Dowdy (4). The following observations on clinical and pathological findings in the macaque subjected to total-body x-irradiation are given to help fill this gap between the knowledge on lower animals and man. Hematologic and electroencephalographic findings in these same animals have been presented in detail elsewhere (5, 6).

### METHOD

Thirty-seven monkeys (*Macaca mulatta*) of both sexes and weighing from 5 to 7 pounds were irradiated. Non-irradiated animals were used for comparison in interpreting autopsy findings and as controls for the detection of epidemics within the colony. Only healthy animals were used and all but 10 had been tuberculin-tested. They were caged separately and fed on a balanced mash diet supplemented with ascorbic acid. They received no antibiotics or parenteral fluids. For two to eight weeks prior to irradiation and during the survival period after irradiation, daily notes were taken of behavior, appetite, and character of stools. Physical examinations were made before irradiation, two to three times per week during the immediate post-irradiation period, and less frequently thereafter. These included observations on general nutrition and activity, on skin,



Fig. 1. Rotating chair and plastic box used to expose animal uniformly to x-ray beam.

hair, conjunctivae, oral and anal orifices, regional lymph nodes, and on liver size. Necropsy examinations were performed, of which only the gross results are presented here.

Non-metallic restraints were used during irradiation to hold the unanesthetized animal in a wooden seat, which was enclosed by a 1 × 1 × 3-foot box of 1/8-inch plastic, liberally supplied with holes for ventilation (Fig. 1). To insure even exposure, the box was turned by a motor at a rate of 1 r.p.m. Control animals confined in this manner and revolved for two hours showed no ill effects.

The axis of rotation of the animal was 100 cm. from the horizontally directed outlet of a 250-kv. G.E. Maximar x-ray unit. Employing 15 ma. with 0.5 mm. Cu and 1.0 mm. Al filters, the half-value layer was

<sup>1</sup> From the Department of Anatomy, School of Medicine, University of California at Los Angeles, and the Veterans Administration Hospital, Long Beach, Calif. Aided by a grant from the National Cancer Institute, U. S. Public Health Service. Accepted for publication in December 1952.

<sup>2</sup> Markle Scholar in Medical Science.

determined to be 1.7 mm. Cu. Variation in intensity in different parts of the field as measured by five calibrated thimble chambers (100 r) was less than 4 per cent of the mean value. Runs made with a calibrated thimble chamber inserted in an axial hole in a masonite cylinder 8 cm. in diameter and 15 cm. long, and rotated in the plastic box, indicated a dosage rate of 13.7 r/min. Monkeys received single doses

handling, and other procedures. However, under these circumstances, 2 of the 8 monkeys receiving doses of 400 r, 3 of 7 receiving 600 r, 9 of 10 receiving 700 r, and 5 of 6 receiving 800 r, died within the first month after irradiation. From this, it would seem that for the monkey the LD 50/30 days is approximately 600 r, while the LD 100/30 days lies close to 800 r (Table I).

TABLE I: SUMMARY OF CLINICAL COURSE OF MONKEYS SUBJECTED TO VARIOUS DOSES OF TOTAL-BODY ROENTGEN IRRADIATION\*

Dose (r)	Number	Died In 30 Days	Survival Time —Days—		Initial			
			Range	Mean	Vomiting	Diarrhea	Hemorrhages	Ulcers
400	8	2	9, 14	11.5	0	+	+	++
550	1	0	....	....	0	++	++	++
600	7	3	13, 13, 20	15.3	+	++	++	+
700	10	9	5, 9-22	12.7	....	++++	++++	...
800	6	5	3-6, 10	5.8	++	++++	....	...

\* Five other animals which were killed within thirty days are not included in the longevity figures.

of 400 r (8 animals), 550 r (1 animal), 600 r (10 animals), 700 r (12 animals), or 800 r (6 animals).<sup>3</sup>

#### RESULTS

The range of dosages used in these experiments extended from a level that killed but a small percentage of animals to one that was almost always fatal. Over much of this range, certain syndromes were manifested, which varied in their severity at the different dosages, although a rather typical course of illness could be recognized at each level. This presentation will first consider the dose-lethality relationships, then each major syndrome, and finally review the course of illness at each dosage level.

##### A. Mortality

Conditions required for rigorous determinations of dose-lethality curves have not been met in these experiments, since the animals were subjected to capture,

Survival times of animals dying within the first month show further relationships to dosage (Fig. 2). With one exception, animals that received 400 to 700 r died nine to twenty-two days after irradiation. In contrast, members of the 800 r group died in from three to five days, 1 other dying at ten days. Thus, survival times following lighter doses are distinct from those after 800 r, and the question may be raised as to whether identical factors are prominent in causing death at different dosage levels.

Of 8 animals which survived the first month, 2 (600 r) are still alive at seven months and 1 (550 r) is alive at 1.2 months after irradiation, the others having died at 1.2, 1.3, 2.0, 3.1 and 4.7 months. Although approximately equal numbers of males and females were included in each group, no differences in length of survival or degree of morbidity between the sexes were found.

##### B. Clinical and Pathological Findings

The overall behavior of the animals will be described first; then, in the order of their importance, the gastrointestinal, hemorrhagic, and other manifestations will be discussed (Table I).

<sup>3</sup> Calibrations were performed by Dr. M. A. Greenfield, Department of Radiology, School of Medicine, University of California at Los Angeles, and irradiations were carried out under the supervision of Dr. R. E. Ottoman, Department of Radiology, Long Beach Veterans Hospital, Long Beach, Calif. Gratitude and appreciation are expressed for the cooperation of these workers.



# SINGLE DOSE, DEEP X-IRRADIATION OF MONKEYS ROENTGENS VS LONGEVITY

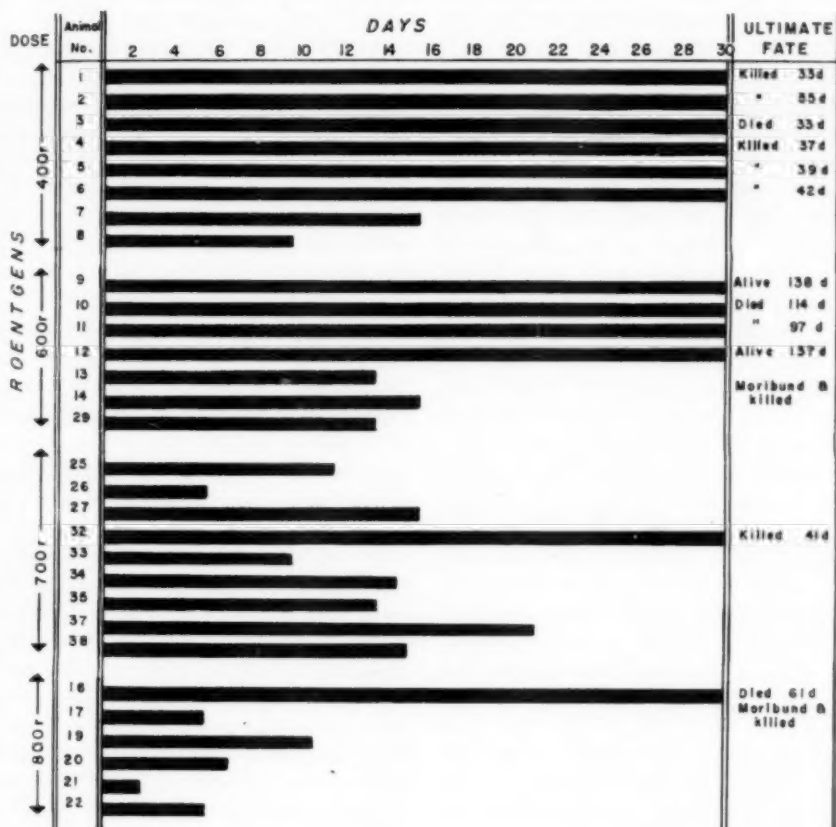


Fig. 2. Survival times of monkeys after 400, 600, 700, and 800 r doses of irradiation (only thirty-day period is graphed).

1. *Behavior:* Most monkeys did not seem in the least affected while being irradiated. Wakefulness, vocalization, grimacing, fingering of surroundings, and occasional struggling continued unabated. Activity and strength seemed usual upon return to their cages. Only when vomiting occurred (see below) were their usual boisterous spirits subdued briefly, and often but momentarily. Similarly, during the early post-irradiation period, no changes in behavior were discernible either upon unobtrusive or closer examination. Hyperactivity, which was looked for because of the excitement stages sometimes seen in

other animals after heavier doses of radiation (7, 8), was not seen.

With the onset of anorexia and loose stools, however, behavior was noted to alter. Although the animals were alert, curious, and vigorous when given close attention, there was, nevertheless, some subduing of their normal restlessness. As diarrhea progressed, this attitude deepened into spiritlessness, from which the animal could be aroused only, for example, by the prospect of escape. Bananas were accepted but only tasted. Movements became slow and weak and appeared to require unusual effort. The animals sat in

a crouched, head-bent position even when free on the floor. Great thirst was manifest, and dehydration was obvious. In final stages, they lay prostrate and became intermittently comatose and hyperpneic before dying.

In animals that recovered, normal alertness and strength were regained with return of appetite and formed stools, and 5 monkeys were noted to exhibit normal behavior from one to seven months after their initial illness. Distinctive personalities of several animals, which were well recognized prior to irradiation, have not been observed to alter for periods up to seven months after irradiation.

*2. Digestive Disturbances:* Most conspicuous among symptoms at all radiation levels were disturbances in digestive function. In most animals of the 800 r group, vomiting, sometimes presaged by closing of the eyes and yawning, commenced during irradiation, while all of the 600 r group vomited within one hour of irradiation. It is doubtful that nausea was prolonged, if present at all, as most animals stopped their activities only briefly and showed apparent relish for food shortly after emesis. Monkeys in the 400 and 700 r groups did not vomit. The unexpected absence of this symptom in the 700 r group is perhaps explained by the fact that these animals were not fed for several hours before irradiation, as the others had been.

A symptom-free period following irradiation, in which almost all animals had undiminished appetites and normal bowel habits, lasted only two to three days in the 800 and 700 r groups and three to five days in the 600 and 400 r animals. The ensuing appearance of gastrointestinal disturbance was introduced by failing appetite and loose stools, followed by complete anorexia with diarrhea or, in several heavily irradiated animals, dysentery. The diarrhea was mild in some of the animals given 400 r, consisting only of loose stools for a day or two. The opposite extreme was manifested following 700 and 800 r, some monkeys recovering

from profuse diarrhea lasting a week and others succumbing. Animals in the 800 r group exhibited the most intense diarrhea, some dying as early as one to three days after its onset, with an average loss of 21 per cent of the body weight. Stools were not noted to be excessively mucoid. All animals that died within fifteen days after irradiation had anorexia and profuse diarrhea at the time of death, and no animal that had diarrhea longer than a week survived the first month. Two instances of vomiting during this period were suspected but not actually observed.

Animals succumbing early—the so-called “acute intestinal death” (9)—revealed no abnormalities of the mouth or esophagus upon postmortem examination. The lower digestive tract was generally emptied of solid material but contained small amounts of fluid. Gut walls in fresh specimens had good tone and were only slightly edematous. The mucosa of the stomach, small intestine and, particularly, the ascending colon was covered by an opalescent mucoid discharge. Signs of bleeding, however, were minimal or absent and submucosal hemorrhages were first encountered at autopsy after deaths during the second week. Occasional round bluish areas, which slightly raised the submucosa of the ascending colon, have been seen in non-irradiated animals also; these are possibly caused by parasites (10).

Three animals which recovered from the initial disturbance and lived for two to four months in apparent good health again became anorexic. A week later, diarrhea began and culminated in death similar to that described following the gastrointestinal disturbances of the acute period. A few submucosal petechiae and ecchymoses were found at autopsy in the stomachs and intestines, although other organs were not grossly abnormal. The deaths of these monkeys, while staggered at 2.0, 3.3, and 4.6 months after irradiation, all occurred within a two-week span. Although neighboring control animals did not become ill, the possibility exists that these deaths were due to an infectious

enteritis rather than to late effects of irradiation, since extreme emaciation, reported by Prosser (11) to occur in subacute deaths of dogs and rabbits after ionizing irradiation, was not seen. A blood sample taken two days before death in one of the animals showed almost complete replacement of neutrophils and lymphocytes by atypical monocytes, a change suggestive of monocytic leukemia (5), which may have been responsible for death.<sup>4</sup>

3. *Hemorrhagic Tendency:* In the course of this study, animal groups were subjected successively to 400, 600, and 800 r, in that order. In view of the well known bleeding tendencies in radiation sickness, it seemed unusual that no skin petechiae were seen and that bleeding elsewhere was usually limited in these animals. Upon subsequently running a 700 r group, however, skin petechiae and widespread bleeding were observed in each of the 4 animals that died fourteen to twenty-two days after irradiation. In 2 macaques in the 700 and 800 r groups which survived the first month, skin petechiae did not develop, an observation which suggests that this bleeding manifestation may have prognostic value.

The fully developed hemorrhagic picture can probably be illustrated best by quoting from the autopsy record of a monkey (No. 28) that died fifteen days after x-irradiation with 700 r and was autopsied one hour after death.

"Emaciated animal, which had been very ill for several days and, for the last day, comatose. Diarrhea profuse but not bloody. Profuse petechiae over scalp, abdomen, thorax, thighs, and forearms. Calf of left leg (where Nembutal injection had been made a week ago) has  $1 \times 2$  cm. hematoma with beginning sloughing of overlying necrotic skin. No conjunctival

hemorrhages. A few petechiae on gums, soft palate, and tip of tongue. Cervical, axillary, and inguinal nodes enlarged to 2-3 mm. and upon dissection almost black. No retro-orbital or nasal cavity hemorrhage seen, though monkey had slightly blood-tinged nasal discharge terminally. Hemorrhage in socket of unerupted molar. No excess thoracic or pericardial fluid. Scattered over both lungs are a dozen 2-5 mm. fairly sharply outlined dark red areas with slightly increased consistency, and at one of these areas there are early fibrinous pleural adhesions. Intervening lung tissue not remarkable. Several parietal pleural ecchymoses. Auricles of heart have numerous diffuse hemorrhages. Pharynx, larynx, tonsils, and upper esophagus not remarkable. Numerous peritoneal hemorrhages. No excess fluid. Stomach has many pinpoint petechiae, especially toward pyloric end. Several diffuse encircling dark hemorrhages 0.5 to 2 cm. broad in walls of intestine and colon, particularly cecum. No ulceration. No blood in lumen. Peri-adrenal hemorrhage on right. Kidneys appear normal. Bladder negative. Liver and spleen not remarkable. A few fine petechiae along epididymis. Mesenteric nodes are enlarged and dark. Cerebrospinal fluid clear. Brain shrunken slightly from calvarium. Meninges and surface of hemisphere not remarkable. Lumbar cord normal."

In 2 other of the more severely hemorrhagic animals, extensive bleeding into subcutaneous tissues and fascial planes was noted and, in one, the colon contained much blood. Hematuria and probable vaginal bleeding were each noticed once. The heart, which is believed to be extremely resistant to direct x-irradiation (12), exhibited hemorrhages in several cases, thus emphasizing the general nature of the bleeding tendency. By contrast, the brain, spinal cord, and meninges never exhibited hemorrhage, and terminal cerebrospinal fluid samples from a half dozen animals were always clear and colorless.

<sup>4</sup> The patterns of response of the monkey's blood elements following irradiation agree broadly with those which have been described for other animals. The general finding consists of a fall in circulating leukocytes in the first few days and their sustained depression during the first month, with subsequent return to normal in surviving cases. Temporal and quantitative features of these changes are specific for the different blood cells (5).

The general hemorrhagic picture was distinctly best developed in five 700 r animals that succumbed from the ninth to the fifteenth day after irradiation. Another 700 r animal, dying later, was found to have several "old" hemorrhages in the lungs and ascending colon and about the kidneys. Lesser evidences of hemorrhage were seen in one 800 r monkey at nine days and in two 600 r animals which succumbed at thirteen and fifteen days. One 400 r monkey dying at nine days had, as sole evidence of bleeding, a single submucosal hemorrhage with ulceration encircling the ileum for about 6 cm. of its length. Another animal of the 400 r group, dying at fifteen days, had no hemorrhages. As noted above, of 7 animals which died four to five days after doses of 600, 700 or 800 r, 4 showed no evidence of hemorrhage and the others had minimal petechiae or ecchymoses of the gastrointestinal tract, chiefly of the ascending colon.

In summary, these data indicate that monkeys dying within four to five days after irradiation, even with 800 r doses, show little bleeding. Hemorrhages were most prevalent at from nine to fifteen days, especially in animals surviving 700 and 800 r. The digestive tract, particularly the ascending colon, gives evidence of the bleeding tendency earliest. In animals displaying the greatest hemorrhagic tendency, bleeding was widespread throughout the body, only the central nervous system being spared. This period of greatest hemorrhagic tendency during the second week was coincident with that of maximal platelet depression but, in 4 monkeys with platelet counts below 40,000 during the second week, no evidence of hemorrhage was observed (5). Other factors, therefore, such as heparin release and increased capillary fragility, are probably involved.

4. *Respiratory Findings:* A few animals were observed to cough after irradiation, and dyspnea and occasionally rhinorrhea were noted preterminally. In a number of animals dying during the hemorrhagic

phase, autopsy revealed up to a dozen fairly sharply outlined 2- to 5-mm. spots of hemorrhage in each lung. Some of the larger of these may have been the sites of bronchopneumonia. In a few cases, 1- to 2-mm. whitish nodules (which may have been arrested tuberculous foci) formed the center of such hemorrhages. In 3 animals dying after the first month, such nodules were found to be ringed by a reddish areola.

5. *Cutaneous Infection and Ulceration:* A characteristic post-irradiation finding in 5 animals was the appearance during the second to third week of two to a dozen small (2 mm.) ulcers on the dorsum of the wrists and digits. Typically these had a punched-out center with a moist, dirty gray base and raised firm margins. There was little associated inflammation and no regional node enlargement. Petechiae were present in only 1 of these animals. In 2 the ulcers healed within ten days, whereas in 3 others they persisted without enlargement until death, which ensued fifteen, thirty-three, and forty-two days after irradiation.

Because these ulcers occurred during a period of red cell abnormality and somewhat resembled those of sickle-cell anemia in location and appearance (13), a test for sickling of erythrocytes was performed in 1 monkey with ulcers but was negative. It seems more likely that the ulcers were traumatic in origin. They showed little inflammation and healing was retarded because of the coexistent leukopenia during their early development. Such an explanation has already been suggested for the absence of inflammation about ulcers in human casualties of atomic bombing. Other infective processes included a large burrowing ulcer of the scalp in 1 animal and a shallow ulcer of the lip in another, each appearing during the third week.

6. *Neurologic Findings:* Particular attention was given to possible neurologic alterations in these animals but, except for non-specific depression of iridal and tendon reflexes, and weakness and labored movement in the severely ill animals, no devia-



tion from normal was encountered. Except for occasional slowing of alpha-wave frequency and more marked changes immediately before death, electroencephalographic studies on 27 of these irradiated monkeys were negative (6).

7. *Other Findings:* Some animals were thought to have slight reddening of the face after irradiation. Hair was shed to a slight degree at fourteen days in all of the 600 r group, but thinning of the hair was not obvious. Subcutaneous edema was not noted. No liver enlargement was felt on clinical examination, nor were there any instances of excess fluid in body cavities. Electrocardiograms of eight 400 r monkeys taken one day after irradiation showed no disturbances of rhythm (cf. 14).

#### DISCUSSION

From the general physiological maxim that data obtained on one species hold true to a degree for other species, especially those closely related, it seems reasonable that radiobiological data from subhuman primates should be most directly applicable to man. Yet Cantril (15) in discussing this question rightly stresses the need of great caution in extrapolating from one species to another, and radiosensitivity even between strains of a single species has been found to differ markedly (8). Both the principle of interspecies applicability and the need for caution and experience have been illustrated by our data.

The dosage lethality curve of the monkey apparently has its LD 50 point at about 600 r and its LD 100 near 800 r. Considering the small number of monkeys used, this value, though somewhat higher, is not exceedingly discrepant with that of 500 r found in a group of monkeys by Dowdy (4) and with the estimated LD 50 values of 400 to 500 r for man (16, 17). Both the monkey and man appear to lie in the median reaches of the spectrum of species radiosensitivity. It should be recognized, however, that estimates for man have been obtained with dosage rates which differ markedly from those of the present experiments, and rates of irradiation

TABLE II. MEAN SURVIVAL TIME (IN DAYS) OF SEVERAL SPECIES OF ANIMALS AFTER MODERATE AND HIGH DOSES OF IRRADIATION

Animal	Reference	Mean Survival Time Days	
		Moderate Dose	High Dose
Monkey	Present study	13	5.8 (800 r)
Dog	Cronkite (18)	12.2	3.3 (3000 r)
Goat	Cronkite (19)	11.5	4.3
Rabbit	Hagen (20)	10	5-6 (>1000 r)
Mouse	Cronkite (18)	11	4-5 (>1500 r)
Mouse	Bonét-Maury and Patti (7)	....	3.2 (>800 r)
Mouse	Quastler (9)	11.5	3.5 (>1500 r)

are known to be influential in modifying the dosage-lethality curve.

Dosage-survival times in the monkey seem to fit a stepped curve such as has been found for other animals (9). When the mean survival times are arranged as in Table II, it is seen that the monkey, like other animals, succumbs three to six days after irradiation above a critical level and eleven to thirteen days after lesser doses. These survival times, corresponding to steps on the dosage-lethality curve, are broadly correlated with distinctive phases in the succession of physiological changes that follow near-lethal irradiation (11).

These phases are as clear in the monkey as in the dog and rabbit and begin during the period of radiation itself. Vomiting and the lessened activity momentarily associated with it are the only initial effects seen in the monkey, as in the dog (11); the shock-like picture encountered in the rabbit is absent. As is true also in man (21), after a short symptomless phase, the period of digestive symptomatology begins. Anorexia, diarrhea, and weakness become severe in heavily irradiated animals, and the first wave of so-called "acute intestinal deaths" occurs. Data on deaths within the first week after the atomic bombings are scarce. However, there are accounts of "mysterious" deaths occurring on the third day associated with severe diarrhea and fever (22).

With intermediate dosages, this early period of gastrointestinal symptomatology runs without sharp separation into a phase characterized by hemorrhages and in-

fections. The total white count, which dropped during the earlier stages, had now reached its maximal depression (5). A second wave of deaths occurred during this period in our monkeys, as is true also of other animals and man.

Monkeys that have survived these critical stages then proceed to recover slowly. Subacute deaths, scattered in time, may still continue to occur over the next few months. In the present experiments, these subacute deaths were preceded by a short period of anorexia and diarrhea. It follows, then, that radiation sickness in the monkey falls into the pattern described for other animals.

Two of the criteria employed in screening a human population for exposure to irradiation have been epilation and cutaneous hemorrhages. Epilation was minimal in our monkeys, and hemorrhage, encountered after radiation at 700 r, was not conspicuous at other dosages in the lethal range. In the present study, it was clear that animals could receive a lethal dose of radiation without showing obvious evidence of bleeding. From the available experience in monkeys, it would appear that alterations in the blood picture may be a more sensitive criterion of exposure to radiation in man (5), though obviously not one readily applicable to a large population.

#### SUMMARY

Features of radiation sickness in a sub-human primate have been obtained from clinical and physiological observations in a series of monkeys subjected to single exposures of total-body x-irradiation at several dosage levels.

Dosage-mortality data for the monkey indicate that the LD 50/30 days is about 600 r, while the LD 100/30 days lies near 800 r. In the monkey, conspicuous phases of radiation sickness include vomiting during irradiation, a symptomless stage after irradiation, a period of gastrointestinal disturbances, and a period of hemorrhage and infection, followed by convalescence. Early deaths occurred in two

waves associated with the gastrointestinal and with the hemorrhagic phases. Later deaths were scattered.

In the monkey, epilation and cutaneous hemorrhages are not present with sufficient regularity to serve as exclusive criteria for exposure to radiation within the lethal range. Alterations in the blood picture, determined in these animals and reported elsewhere, appeared to be the most sensitive index.

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#### SUMARIO

##### La Enfermedad por Irradiación en el Mono

Estas observaciones clínicas y fisiológicas fueron llevadas a cabo en monos expuestos a dosis únicas de irradiación roentgen de todo el cuerpo, que variaban de 400 a 800 r. A juzgar por estos estudios, parece que para un período de treinta días la DL 50 para el mono es de unos 600 r, en tanto que la DL 100 se aproxima a 800 r. Con una excepción, las muertes consecutivas a dosis de 400 a 700 r tuvieron lugar de nueve a veintidós días después de la irradiación, mientras que los animales que recibieron 800 r murieron en término de tres a cinco días.

La enfermedad por irradiación mostró en general la siguiente evolución: vómitos durante la irradiación o inmediatamente después, seguidos de una etapa asintomática que duró de dos a cinco días, con aparición subsiguiente de trastornos gastrointestinales (inapetencia, diarrea) y más tarde signos de hemorragia e infección. El período de mayor diátesis hemorrágica coincidió con el de trombocitopenia máxi-

ma. En algunos animales, hubo ulceración cutánea. No se observaron depilación ni hemorragias cutáneas.

Los graves trastornos digestivos que siguieron al breve intervalo asintomático en los animales que recibieron dosis altas dieron por resultado la primera onda de las llamadas "muertes intestinales agudas." Con las dosis intermedias, ese período temprano de semiología gastrointestinal pasó sin demarcación neta a la fase de hemorragia e infección, sobreviniendo otra onda de mortalidad. Los monos que sobrevivieron esos períodos críticos procedieron, en su mayor parte, a reponerse lentamente.

A juzgar por estas observaciones, parece que la depilación y las dermatorragias acaso sean pautas menos seguras de la exposición a la irradiación dentro de límites letales que las alteraciones del cuadro sanguíneo, que según se observó, convinieron toscamente en estos animales con las descritas para otras especies.



# The Dosimetry of Beta Radiations<sup>1</sup>

ROBERT LOEVINGER, Ph.D

WITH UNIFORM distributions of beta emitters in large volumes dosimetry is relatively simple, and has been adequately treated by various authors (1, 2). The dosimetry of small or non-uniform sources, on the other hand, has received little attention. It is with the physics aspects of this problem that the present paper is concerned.

The basic physical information required for beta particle dosimetry is the distribution of absorbed energy around a point source of beta particles in an absorbing material. If this point source energy distribution function were known, we could, at least in theory, compute the distribution of absorbed energy for any known distribution of a beta emitter. If such a point source function could be computed for monoenergetic electrons from the theory of scattering and energy loss, it could be integrated with a known beta spectrum to give the point source function for a beta emitter. To date, the computation has not been made in useful form, and an experimental approach must be adopted. Some direct measurements have been made on very small beta sources in air, for which preliminary results only are available (3). The present paper describes measurements made on very thin plane sources, from which the information for a point source can be computed.

The simple theory, along with a statement of preliminary results of measurements on P<sup>32</sup>, has already been published (4). The theory may be briefly stated as follows. If we suppose a point source of beta particles in a homogeneous absorbing medium larger in all directions than the maximum range of the particles, then the absorbed energy per unit volume must be a radially-symmetrical function of distance

from the source. Let this function be represented by  $I(x)$ , and call it the "point source energy distribution function." If now we suppose an infinite thin plane source in the medium, then the distribution of absorbed energy in a direction normal to the plane is given by

$$D(z) = 2\pi \int_z^{R_0} x I(x) dx \quad \text{energy/c.c. per dis/cm.}^2 \quad (1)$$

where  $R_0$  is the maximum beta range,  $z$  is the perpendicular distance to the plane source, and the point source function  $I(x)$  is in units of energy/c.c.-dis. Conversely, it can be shown (4) that if  $D(z)$  is known, then  $I(x)$  can be determined by suitable differentiation:

$$I(x) = \frac{A}{z} \left( -\frac{dD}{dz} \right) \quad (2)$$

where

$$A = \bar{E}/2\pi \int_0^{R_0} D(z) dz \quad (3)$$

$\bar{E}$  being the average energy per disintegration for the beta spectrum. The last equation expresses the condition that the energy absorption takes place in a sphere of radius equal to the maximum beta range,  $R_0$ . Consideration of Equations 2 and 3 shows that the experiment need give only relative values of  $D(z)$ , since multiplying  $D$  by any constant does not change the value of  $I(x)$  computed according to Equation 2.

Now it is feasible to make a thin plane source, and measurements can be made of absorption in planes parallel to it. Measurements of this type have been made on a number of beta emitters, using a variable-spacing, parallel-plate ionization chamber, usually referred to as an extrapolation chamber. This instrument, devised by Failla many years ago (5, 6,) is ideally suited

<sup>1</sup> From the Physics Laboratory and Department of Radiotherapy, Mt. Sinai Hospital, New York, N. Y. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.



to this experiment, which calls for plane parallel geometry. The extrapolation chamber measures ionization in air, and it will be assumed, without an attempt at justification, that ionization measurements are proportional to absorbed energy (7). Thus, in this paper "absorbed energy per c.c." is to be understood to have the operational meaning of "observed ionization per c.c. in a vanishingly small air cavity."

The experimental measurements on thin plane sources will be given (Figs. 3, 4, and 5) after a simple equation has been presented with which they can be compared. The point source distribution function which has been deduced from the measurements apparently has the same form for all the isotopes observed, and represents the measurements well from the nearest distance to the source out to the end of the range. This function  $I(x)$  is a two-part function, which may be written as follows (Equations 4 and 5):

$$I_1(x) = k/(\nu x)^2 \quad \text{for } x \leq 1/\nu \quad (4)$$

$$I_2(x) = \frac{k}{(\nu x)^2} \frac{\nu x \exp(1 - \nu x) - \nu R_0 \exp(1 - \nu R_0)}{1 - \nu R_0 \exp(1 - \nu R_0)} \quad \text{for } 1/\nu \leq x \leq R_0 \quad (5)^2$$

$$r^2 I_1(r) = k \quad \text{for } r \leq 1 \quad (6)$$

$$r^2 I_2(r) = k \frac{r \exp(1 - r) - R \exp(1 - R)}{1 - R \exp(1 - R)} \quad \text{for } 1 \leq r \leq R \quad (7)$$

Here (Eqs. 4 and 5),  $\nu$  is the experimentally observed "total-scatter attenuation coefficient," and  $k$  is a normalizing factor computed from the average energy per disintegration. The two parts  $I_1$  and  $I_2$  join smoothly and continuously at the joining point  $1/\nu$ . The attenuation coefficient,  $\nu$ , and the maximum beta range,  $R_0$ , are experimentally found to be functions of the maximum energy of the beta spectrum, which thus determines the geometrical distribution of the absorbed energy. These equations apply to a point source in a uniform absorbing medium which is larger than the maximum beta range in all direc-

tions from the source, which is called here a situation of "total scatter."

It is seen that in the two equations for  $I(x)$ , distance appears only in the dimensionless form  $\nu x$  and  $\nu R_0$ . If now the distance,  $x$ , and the range,  $R_0$ , are expressed in multiples of  $1/\nu$ , then  $\nu$  disappears from the equations, which can then be rewritten in the simpler form of Equations 6 and 7, where now  $r = \nu x$ ,  $R = \nu R_0$ , and the joining point for the two parts has become unity. In order to simplify the appearance of the equations, they have been multiplied through by  $r^2$ , which in effect puts the inverse-square part of the function (which is purely geometrical in origin) on their left-hand side. These geometrically dimensionless equations are simpler to read and write than the full equations, and will be used in the remainder of the discussion. The full dimensional equations can be obtained at any step simply by multiplying each dimensionless distance by the unit of distance,  $1/\nu$ .

By applying the condition that the average energy per disintegration  $\bar{E}$  is absorbed within a sphere of radius  $R_0$ , the constant  $k$  is determined as

$$k = \frac{\nu^3 \bar{E}}{12\pi} \frac{1 - R \exp(1 - R)}{1 - \frac{1}{3}(R^2 + R + 1) \exp(1 - R)} \quad (8)$$

The product  $\nu R_0 = R$  will be called the "dimensionless range" of the beta spectrum and it will be seen to be approximately constant.

Perhaps the most notable feature of the energy distribution is that it shows pure inverse-square attenuation out to the joining point of the two-part function. Apparently absorption of the beta particles is

<sup>2</sup> The exponential function  $e^x$  will be given in the form  $\exp(x)$  to simplify the writing of the more complicated equations.

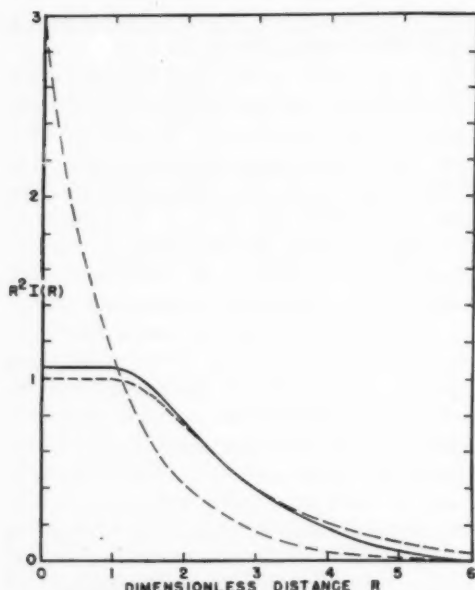


Fig. 1. Comparison of three point source energy distribution functions, normalized to the same area. The solid curve represents Equations 6 and 7 for  $R = 6$ . The dashed curve of similar shape represents Equations 9 and 10. The highest curve represents the conventional assumption, Equation 11.

just balanced by scattering, leaving only the geometrical part of the attenuation process. Beyond the joining point, the fall-off is more rapid than inverse square, the absorbed energy, of course, going to zero at the end of the beta range. If  $\bar{E}$  in Equation 8 has the units energy/disintegration, and  $\nu$  has the units  $\text{cm.}^{-1}$ , then  $k$  has the units energy/c.c.-dis., since  $R$  is dimensionless. Then Equations 6 and 7 may be called geometrically dimensionless, even though  $I_1$  and  $I_2$  carry the units of  $k$ . The dimensionless range,  $R$ , is the actual linear range  $R_0$  multiplied by the coefficient  $\nu$ , and it will be seen below to have values ranging from about 4.5 to 8.0. If we suppose the beta range to become infinite, then the end-of-the-range terms  $\exp(1-R)$  vanish in Equations 7 and 8. Then the Equations 6, 7, and 8 can be written in the simpler form already published (4):

$$r^2 I_1 = \frac{\nu^3 \bar{E}}{12\pi} \quad \text{for } r \leq 1 \quad (9)$$

$$r^2 I_2 = \frac{\nu^3 \bar{E}}{12\pi} r e^{1-r} \quad \text{for } 1 \leq r \quad (10)$$

For most medical and biological dosage calculations, interest is directed to the region of high dosage. Since, in general, intensity falls to about 1 per cent at half the maximum beta range, Equations 9 and 10 can be used. The mathematical manipulations are, of course, simpler without the end-of-the-range terms.

In published calculations on beta dosage from small sources, it has been customary to assume that the point source function for beta sources shows inverse-square attenuation with exponential absorption superposed on it (8). In the symbols already introduced, this leads to an equation of the form

$$r^2 I(r) = \frac{\nu^3 \bar{E}}{4\pi} e^{-r} \quad (11)$$

a single equation of the same geometrically dimensionless form. In the absence of experimental information, this is a reasonable form to assume.

Figure 1 compares the three point source functions graphically. It is seen there that, for a given value of  $\nu$ , Equation 11 overestimates the absorbed energy at small distances by a factor of about 3. It is a reasonable supposition that this would not be confused with the form proposed in this paper, in a carefully designed experiment. It will be shown below that the difference between the curves for  $R = 6$  and  $R = \infty$  results in a marked difference in the shape of the absorption curve near the end of the beta range.

By substituting in Equation 1 the value of  $I(x)$  from Equations 6 and 7, and carrying out the indicated integration, we can deduce the following formulas for the distribution of the absorbed energy normal to a thin plane source (except for a multiplicative constant):

$$D_1(z) = B - C \log_e z \quad \text{for } z \leq 1 \quad (12)$$

$$D_2(z) = e^{1-z} - e^{1-R} - (1-C) \log_e (R/z) \quad \text{for } 1 \leq z \leq R \quad (13)$$

Here  $D_1$  and  $D_2$  are the two parts of the predicted attenuation curve  $D(z)$  for a thin source,  $z$  is the perpendicular distance to the plane in the dimensionless units al-

ready introduced. The constants are given by

$$B = 1 - (1 + R \log_e R) e^{1-R} \quad \text{and} \\ C = 1 - R e^{1-R} \quad (14)$$

$D_1$  is evidently a logarithmic function of  $z$ .  $D_2$  is an exponential function of  $z$ , minus two terms which are small compared to the

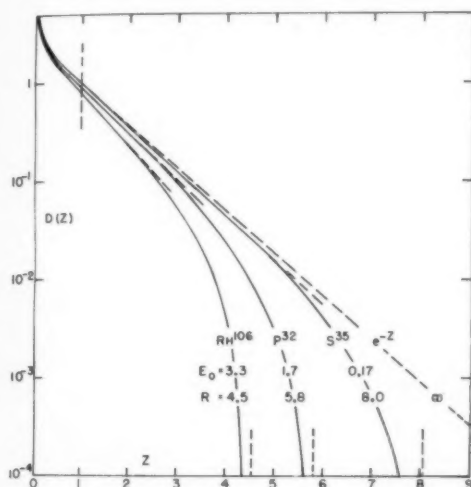


Fig. 2. Total scatter attenuation curves for thin plane sources. Curves are calculated from Equations 12 and 13 for the values of  $R$  shown. The dotted vertical lines at the bottom of the figure correspond to the values of  $R$ , and indicate the maximum ranges. The curves give  $D_1$  for  $z \leq 1$ , and  $D_2$  for  $1 \leq z$ .  $D_1$  and  $D_2$  are seen to join smoothly.

exponential when  $z$  is near unity, but which become relatively large as  $z$  approaches  $R$ .  $D_2$  vanishes at  $z = R$ . Calculated curves from these equations are given in Figure 2 for three values of  $R$ , the dimensionless range. These values correspond to those for the three isotopes indicated in the figure. Now, these curves apply strictly only to infinitely thin plane sources in an absorbing medium larger than the maximum beta range in all directions from the point of measurement. We might refer to them as "total scatter attenuation curves." But it will be noted that they have the same general shape as the absorption curves of beta sources taken with Geiger counters. It is characteristic of such curves to show an exponential region, followed by a downward concavity near the end of the range.

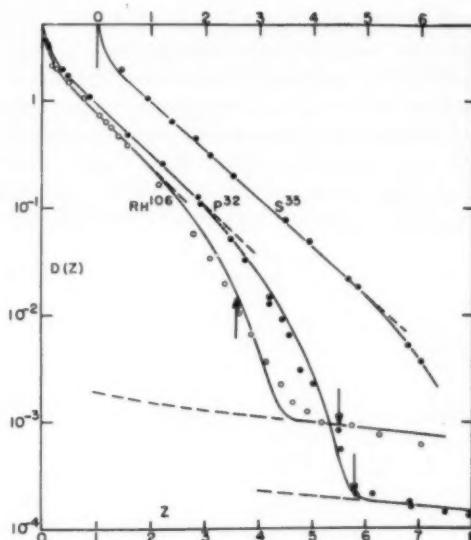


Fig. 3. Exponential plot of computed total scatter attenuation curves for thin plane sources and experimental points for three isotopes. The arrows indicate the maximum (dimensionless) ranges. ( $Rh^{106}$  has two components.) Polystyrene was the absorbing and scattering material for the experimental points. The  $S^{35}$  curve has been shifted one unit to the right, for clarity.

It has also been known that the softer spectra show longer exponential sections than the harder (9). We have here an explanation for this phenomenon. The longer exponential portion of the curves arises from a larger dimensionless range, which characterizes the softer spectra. The most energetic spectrum shown, rhodium<sup>106</sup>, with the smallest dimensionless range, has as a result the shortest exponential region. The function  $D_1$  is concave upward on an exponential graph, the function  $D_2$  is concave downward. They join with a flex point at  $z = 1$ . The exponential region is the tangent at the point of flexion.

The dimensionless ranges used are the product of the actual beta range,  $R_0$ , times the attenuation coefficient,  $\nu$ , determined from measurements shown below. The fact that the dimensionless range decreases with increasing energy means simply that the attenuation coefficient decreases faster than the actual range increases, so the product  $\nu R_0$  decreases with increasing energy

It is tempting to suppose that all softer spectra would show attenuation curves falling between the  $S^{35}$  curve and the limiting curve for  $R = \infty$ , marked  $e^{1-s}$ , but this would be an unwarranted extrapolation.  $S^{35}$  represents the lower limit, and  $Rh^{106}$  the upper limit, of the energies examined experimentally, and all generalizations pre-

lung from the metal applicator.  $Rh^{106}$  is composed of at least two beta spectra. The mean energy was used in the computation, so the observed points are high near the end of the range, where the hard component alone is present.

Similar curves are shown in Figure 4 for three additional isotopes. The RaE meas-

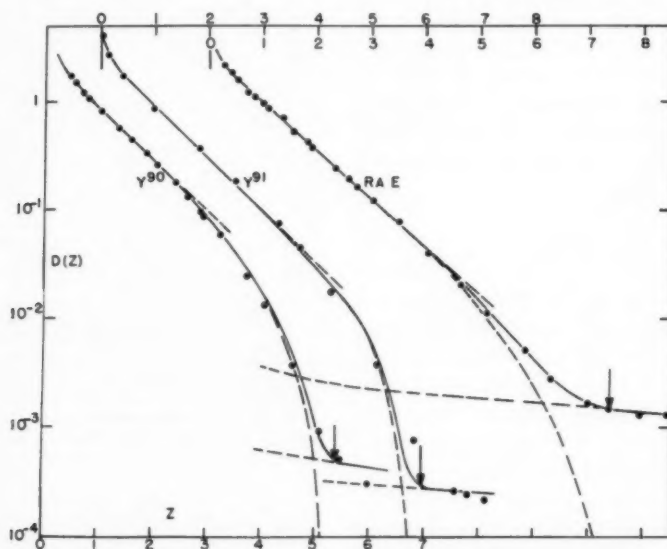


Fig. 4. Same as Fig. 3, for three additional isotopes. The  $Y^{91}$  curve has been shifted one unit, and the RaE curve has been shifted three units to the right.

sented are intended to be limited to this range of energy.

A comparison of the calculated curves with the experimental points is shown in Figures 3, 4, and 5. Figure 3 shows the same three isotopes as Figure 2. To the attenuation curve for  $P^{32}$ , as given in Figure 2, there has been added a bremsstrahlung contribution shown by the straight line at the bottom of the figure. The line shown has been computed from a simple theory, and has been adjusted to fit the curve at the end of the beta range. No bremsstrahlung contribution has been made for  $S^{35}$ . The  $Rh^{106}$  points were taken using a Ru- $Rh^{106}$  ophthalmic applicator (10). The higher background in this case is presumably partly the  $Rh^{106}$  gamma radiation and partly increased bremsstrah-

urements were made with an ophthalmic applicator (11) and show the somewhat higher background due to gamma rays and the increased bremsstrahlung of a metal source. Except for  $Rh^{106}$  and RaE, all sources were mounted on plastic. In fitting each of these curves, the range  $R_0$  in mg./cm.<sup>2</sup> for each spectrum was taken from a recent discussion of the electron range-energy relation (12), assuming that ranges in polystyrene are given by the ranges in aluminum multiplied by the ratio of the electron densities of the two substances. Except for a multiplicative constant, the only adjustable parameter was the attenuation coefficient  $\nu$ . The curves shown are computed, not drawn to fit the points. The accuracy with which the curves do fit the experimental points—



in some cases covering an intensity range of more than  $10^4$ —gives confidence in the correctness of the point source functions proposed here. At the time the measurements were made, it was not anticipated that the shape of the absorption curves near the end of the beta range would be of interest. As a result, the low intensity

of  $z$  less than unity represents the points well. This logarithmic function of distance for a thin plane source indicates a pure inverse square near a point source. It was, in fact, this very striking phenomenon which first called attention to the analysis which has produced the functions presented in this paper.

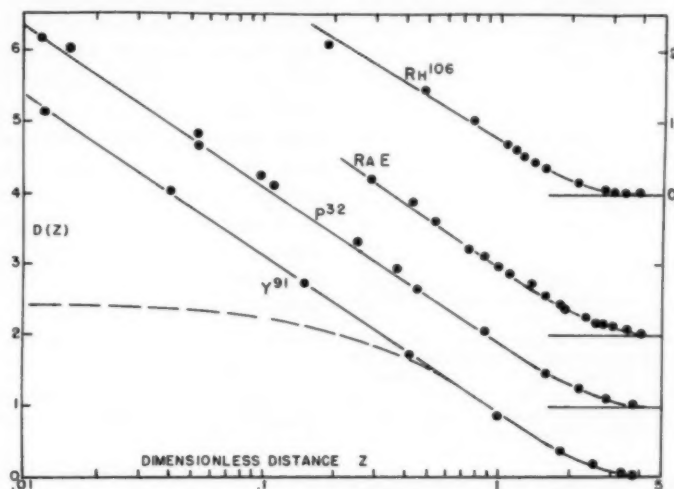


Fig. 5. Logarithmic plot of computed total scatter attenuation curves for thin plane sources and experimental points for four isotopes, for  $z < 4$ . The dotted curve shows, for comparison with the straight line  $D_1(z)$ , the exponential  $D_2(z)$ , for  $Y^{91}$  only. The curve for  $P^{32}$  has been shifted upward one unit,  $RaE$  shifted upward two units, and  $Rh^{106}$  shifted upward four units.

measurements were not made with the sort of care necessary for an accurate range determination. Thus, it seemed appropriate to use published ranges and determine only the attenuation coefficient by fitting the curve. It is clear, however, that a functional form which fits an absorption curve, and which is very sensitive to the value of the maximum beta range, offers an objective method of determining that range.

Figure 5 is a logarithmic plot of the experimental points for those sources which were measured for values of  $z$  less than unity. On the bottom curve, the exponential function has been shown as a dotted line for values of  $z$  less than unity, to indicate the smooth joining of the two functions, which are hardly distinguishable from  $z = 0.5$  to  $z = 1.5$ . The figure shows that the predicted straight line for values

The attenuation coefficients for the six thin-source functions already shown are plotted in Figure 6 against the maximum beta energy  $E_0$ . Also shown there is an attenuation coefficient for thallium<sup>204</sup>, computed from thick-source measurements made by Bailey (13), and also a value from thick-source measurements on calcium<sup>45</sup>. The  $Sr^{90}$  coefficient was deduced from a  $Sr-Y^{90}$  attenuation curve, after subtracting the  $Y^{90}$  contribution. The results are well represented by the straight line shown. Measurements were made in polystyrene in all cases, but have been reduced to  $cm^{-1}$  of water (using the ratio of the electron densities) as a simple standard substance suitable for dosimetric calculations. The results are seen to be well represented by the equation

$$\mu = 18.9 E_0^{-1/3} cm^{-1} \text{ water} \quad (15)$$

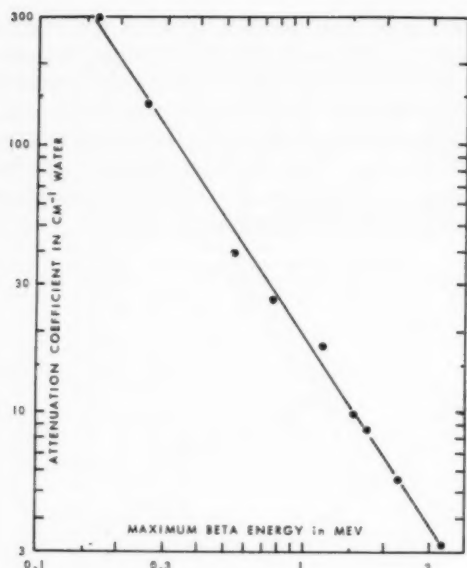


Fig. 6. Total scatter attenuation coefficients  $\mu$  for nine isotopes plotted against the maximum  $\beta$  energy  $E_0$ . The points represent the following isotopes, in order of increasing  $E_0$  (left to right in the figure):  $S^{35}$ ,  $Ca^{48}$ ,  $Sr^{90}$ ,  $Tl^{204}$ ,  $RaE$ ,  $Y^{91}$ ,  $P^{32}$ ,  $Y^{90}$ ,  $Rh^{106}$ .

In the published discussions of beta particle absorption (12, 14), an effective absorption coefficient is usually derived from the exponential part of the absorption curve, and given by an equation of the form

$$\mu \propto E_0^{-n} \quad (16)$$

where  $n$  is given various values from 1.33 to 1.43 by various authors. Now, the slope of the exponential part of the attenuation curves described in the present paper can be found from the derivative of Equation 13, and this result, combined with Equation 15, gives an equation for  $\mu$  agreeing well with equation 16 for  $n = 1.4$ . Thus it is tempting to believe that somehow the exponent of  $E_0$  in Equation 15 should be exactly  $3/2$ , and that this value is realized only when the effect of the finite range of the beta particles is included in the shape of the absorption curve.

The deviations of the values of  $\mu$  (from the straight line of Figure 6) for  $RaE$  and  $Sr^{90}$  appear to be real. These two spectra have a special (forbidden) shape. Perhaps the shape of the beta spectrum is another

parameter controlling the value of the attenuation coefficient. Equation 15, as it now stands, combined with the point source energy distribution functions given above, probably offers sufficient accuracy for all ordinary medical and biological computations of beta dose from distributed sources in and on soft tissue.

Starting with Equations 6, 7, and 8, formulas can be calculated for dose distribution from sources of various sizes and shapes, e.g., plane slabs, disks (on the axis), cones of revolution (on the axis), and spheres. Some of these calculations have been given and illustrated with graphs by Rossi (8), who used Equation 11 as a starting point. Recalculation of his results with the present formulas gives qualitatively the same result, but with some quantitative changes. These results, along with more detailed consideration of the physical aspects of the absorption of beta spectra, will be presented elsewhere in a somewhat more technical paper.

#### SUMMARY

The dosimetry of beta radiation from small sources is shown to depend upon knowledge of the distribution of absorbed energy around a point source of beta particles. The difficulty of making a direct determination of this quantity is discussed. Equations are given for determining this "point source energy distribution function" from measurements on very thin plane beta sources. The results of such measurements on six beta-emitting isotopes are given in the form of a two-part equation. Comparison of this theoretical result with the experimental points is shown in the form of graphs. The theory represents the measurements closely, from very small distances out to the end of the beta range.

NOTE: Since the above was written, the results of Clark and his colleagues have been made available in a personal communication. Study of their data has made it clear that the point source function is a little more complicated than indicated in Equations 4 and 6. It now appears that  $r^2 I_1(r)$  is approximately constant for  $Y^{91}$  and harder isotopes, but is not constant for softer isotopes than  $Y^{91}$ . Thus, Equation 6 is to be considered approximately

correct for the harder isotopes, but incorrect for the softer ones. In view of this, the belief expressed in this article that the point source function described is applicable to all beta-emitting isotopes is now seen to be in part unjustified. A paper containing the most recent results is now in manuscript form and will be submitted for publication in the immediate future.

**ACKNOWLEDGMENTS:** The experimental part of this work was performed under AEC contract At(30-1)-529. The Ra(D + E) ophthalmic applicator was kindly loaned by the Eldorado Mining and Refining (1944) Ltd. The Ru-Rh<sup>106</sup> ophthalmic applicator was kindly loaned by the Atomic Energy Medical Research Project of the Western Reserve University School of Medicine.

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#### SUMARIO

##### La Dosimetría de los Rayos Beta

La dosimetría de la radiación beta procedente de focos pequeños se basa, según se demuestra aquí, en el conocimiento de la distribución de energía absorbida alrededor de un punto focal de partículas beta. Discútese la dificultad encontrada para determinar directamente esa cantidad. Ofrecense ecuaciones para determinar "la función de la distribución de energía del punto focal" por medio de mediciones ejecutadas en focos beta planos y muy delgados. Preséntanse los resultados de esas mediciones en seis núclidos emisores de rayos beta, en forma de una ecuación en dos

partes. La comparación de ese resultado teórico con los puntos experimentales se expone en forma de gráficas. La teoría representa muy aproximadamente las mediciones, desde distancias muy pequeñas hasta el extremo del alcance de los rayos beta. Ofrecense generalizaciones que permiten aplicar el resultado a todos los focos de partículas beta. A la luz de esos resultados, puede calcularse la dosis que reciben los tejidos con cualquier distribución conocida de sustancias radioactivas emisoras de radiación beta, en o sobre los tejidos blandos.

#### DISCUSSION

**G. Failla, Sc.D.** (New York, N. Y.): This is a very good paper and illustrates the value of mathematics in planning and interpreting an experimental investigation. Dr. Loevinger was able to determine the variation of dose with dis-

tance from a point source of beta rays without actually using a point source in his experiments.

The practical applications of this work are rather important. The most pertinent example at a meeting of radiologists is perhaps the dosage

problem in the treatment of the thyroid by externally applied x-rays and by the internal administration of radioactive iodine. Empirically it has been found that the therapeutic tissue dose of x-rays is 2,500 to 3,500 r, whereas calculations of the dose received by the thyroid from the radioiodine accumulated in it indicate that the therapeutic dose in this case is 6,000 to 8,000 rep or "equivalent roentgens." Since most of the tissue dose is delivered by the beta rays of the iodine, it has been assumed by some that the biological effectiveness of the beta rays is less than that of x-rays. In these calculations it has been assumed that the iodine is uniformly distributed in the gland, whereas in fact it is locally concentrated in small regions throughout the tissue. Cells between these "point sources" of radiation then receive much less radiation than those immediately surrounding the sources. To affect these in-between cells, therefore, the dose at shorter distances from the sources must be much larger. This makes the average dose higher than it would be if the iodine were uniformly distributed. The high average dose, therefore, can be accounted for without attributing a lower effectiveness to beta rays. The data presented by Dr. Loevinger will now permit a closer approximation to the effective dose, if one is willing to determine the spatial distribution of the radioactive iodine in the thyroid (*e.g.*, by autoradiographs).

There are many cases in radiobiology in which radioactive material may be concentrated in small regions and the determination of the dose distribution is essential for the correlation of dose and effect.

The same problem is now being investigated in my laboratory by a more direct experimental approach, and it will be interesting to compare the results with Dr. Loevinger's.

**L. D. Marinelli, Ph.D.** (Chicago, Ill.): Some years ago we started experiments designed to measure the ionization in air at different distances from point sources emitting beta rays. These experiments are still continuing, and, therefore, we have not had the opportunity of checking Dr. Loevinger's calculations. I may say, nevertheless, that we do hope to include our results in his all-embracing scheme, since the latter is relatively simple and offers the major advantage of yielding empirically all data necessary in beta ray dosimetry calculations from point sources on the mere knowledge of the energy of the most energetic beta ray in the spectrum. The physicists, of course, would like to derive these formulas from the beta ray spectrum of the source and the laws of electron scattering; in their attempt to do so, they will have the advantage of aiming at Dr. Loevinger's "universal formula," which, we hope, fits the experimental results.





## Education and Training of Health Physicists<sup>1</sup>

ELDA E. ANDERSON

HEALTH PHYSICS is a growing profession. Prior to 1942, experience with radiation hazards was almost wholly associated with the use of radium and x-rays by the medical profession and with experiments in physics laboratories. The employment of x-rays and radioactive materials by industry was quite limited. Many injuries and some deaths occurred during this period which were directly attributable to radiation exposure. This gave impetus to the establishment of "codes" or "standards" for radiation protection, which were of invaluable help in the early days of the Manhattan Project when it was faced with unprecedented radiation hazards. The problem had quickly changed from that of a few radium dial painters following a fixed procedure, and of scientists, doctors, and technicians dealing with small quantities of radium or with x-ray machines and accelerators, to one involving many people working in the vicinity of a nuclear reactor releasing radiation which was of seemingly fantastic magnitude and which consisted, in part, of neutrons whose behavior was little known. To be considered, also, were scientists working with new radioactive materials many times more intense than the usual radium source and with accelerators, the voltages of which had been stepped up by large factors over the earlier models.

These unprecedented problems in radiation hazards encountered in the Manhattan Project were solved by the co-operation of physicists, chemists, biologists, and medical men, and a new group of specialists known by various names, of which the most common was probably "health physicist"—specialists whose problem it is to detect, to control, and to protect against radiation hazards. The constantly expanding atomic energy program (new reactor sites

and new laboratories), the increased use of radioactive isotopes in industry and in research, the new problems in civil and military defense, in industrial hygiene, and in environmental health, have increased the demand for trained health physicists by the Atomic Energy Commission, the U. S. Public Health Service, the National Military Establishment, by industry, by universities, hospitals, and laboratories.

In the older AEC plants, small efficient groups of trained people developed around an exceedingly small number (3 or 4) of individuals who had had experience in the field of radiation hazards prior to the war. In the newer AEC plants, some of the health physicists have been recruited from the staffs of the older plants, while others have been trained either through the AEC Fellowship program or by on-the-job training in one of the established Health Physics Divisions. In any hospital, research laboratory, or industrial organization using radioactive materials, or operating reactors and/or accelerators, it is essential to have available an individual trained in radiation monitoring and in the handling, measurement, and disposal of isotopes and their associated by-products. The degree of training needed by this person will depend on the nature and magnitude of the operations involved.

There is a need for trained people ranging from the equivalent of the plant monitor on the one hand to the responsible and highly trained radiological physicist on the other. Periods of training range all the way from a few weeks on-the-job training to a highly integrated training equivalent to a course leading to a Ph.D. with post-doctoral training. Dividing this wide range of trained people into three groups, (1) the surveyor, (2) the supervisor, or junior health physicist, and (3) the

<sup>1</sup> From the Health Physics Division, Oak Ridge National Laboratory. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

specialist or senior health physicist, let us examine the responsibilities and training of each.

The surveyor who does the routine health physics tasks in the larger health physics organizations cannot be expected to anticipate, measure, and control the many hazards associated with processes involving radioactive materials and sources without knowing why the readings on his meters are meaningless until properly interpreted. He must have an empirical command of the science behind his methods. His training while not extensive must be sufficient to develop proper judgment and an appreciation of the factors involved in interpreting his observations and measurements. He must be capable of checking the performance of his instruments; he must be able to make battery and tube replacements; and he must be fully versed in the detection and measurement of contamination. Such training could be obtained by working in the field (*i.e.*, on-the-job training) under a capable supervisor, the time required to train a surveyor depending on his capabilities, his previous education and training, and his interest. At Oak Ridge, in general, men with at least two years of college training are selected, and preferably those who have shown an interest in science or engineering.

The junior health physicist or the supervisor is the man responsible for radiation control and monitoring beyond the routine stage. The level of training outlined below is minimal for the man who is to work alone, the health physicist who is to be responsible for the radiation protection in the university, hospital, small industrial plant, or research laboratory, or who may be a health physics supervisor in a larger installation, requiring many surveyors. His must be a term of formal work of at least a year and be equivalent in attainment to a master's degree. It is for the purpose of training this type of health physicist that the AEC Graduate Fellowship in Radiological Physics is designed. Since health physics as a practical indus-

trial or laboratory protective effort is approximately 99 per cent physics, chemistry, and engineering, and only about 1 per cent biology, the primary requisite in the selection of these fellows is that they shall have obtained their degrees after majoring in physics, chemistry, or engineering (usually electrical or chemical), with a minor in mathematics, biophysics, or similar field. The AEC Fellow then pursues an academic course at the graduate level for the school year, his course of study tailored to his undergraduate course and planned so as to give him a sound knowledge of atomic and nuclear physics, with emphasis on the interaction of radiation with matter, a fund of specialized biological information, the necessary knowledge in the field of electronics, and, in addition, the integrated body of information that could be referred to as the theory and practice of health physics.

Listing only major topics, this course should include a general appreciation of radiation hazards; the principles of measurement of ionizing radiations; instrumentation, methods of protection; the technic of personnel monitoring, of area monitoring (air, water, mud, plant and animal life, and soil), of building surveys (radiation levels, air contamination, surface contamination); information on design of building and equipment for handling radioactive material, and general health physics calculations (shielding; maximum permissible concentrations of radioactive materials in body, air, water, etc.; radiation dose from external and internal sources). It is this body of information which is currently familiar to relatively few people. Its dissemination is handicapped at the present time, since much of it is not published and, when published, appears generally as a section of a book or in pamphlet form. A query frequently encountered is, "Where can I find material on health physics?"

Following the nine months in formal classroom work, the Fellows spend the remainder of the year in field training, gaining experience in monitoring, surveying, and solving practical problems in

health physics. The installation chosen for field practice must be one where all phases of health physics are encountered, and where the student can be closely associated with the latest technics and developments. Such training programs cannot be properly carried out "just anywhere." There must be ready access to large quantities of radioactive materials, close contact with operations involving radioactive materials, as well as with reactors, accelerators, etc. This field training requires a well planned program where the student works with men of experience in health physics and where he gains the ability to solve health physics problems independently and to gain confidence in his ability to do so. These are the men who will be faced with many different problems in the university physics laboratory, hospital, chemistry laboratory, research laboratory, etc. They must have the information and knowledge to handle these problems, for in most instances they will have no specialist at hand to solve them. They must be able to perform minor repairs and to calibrate their instruments, and must be familiar with the latest instrument developments. They must know how to handle and dispose of radioactive waste products for the small hospital and laboratory and industrial users as well as for large plants. They must be familiar with decontamination procedures, as well as routine monitoring methods and keeping of records. In most instances they must also be diplomats, whose authority comes from accurate knowledge and information.

Out of this group of men, after additional years of experience, one expects to get some of the third class of health physicists, those beyond the level of general supervision, the specialists and senior health physicists, who by training and/or experience have the equivalent of a Ph.D. The man who is to be responsible for the overall radiation safety program in a large plant must have a sound basic knowledge

TABLE I: AEC FELLOWS IN RADIOLOGICAL PHYSICS

AEC installations.....	28
Other government agencies.....	7
Universities and medical schools.....	5
AEC industrial hygiene fellowship.....	1
Graduate work.....	14
Medical school.....	1
AEC project (part-time).....	1
AEC Fellowship extensions.....	10
Present occupation unknown.....	4
<b>TOTAL</b>	<b>59</b>

of mathematics and physics with emphasis on atomic and nuclear physics, a reasonable background knowledge of general and industrial chemistry, electronics, biology and biophysics, and psychology, to which there must be added administrative ability.

The rapid expansion in the nuclear energy field with its increasing use of radioisotopes, high energy accelerators, etc., makes it imperative that due consideration be given to the training of health physicists. No longer can it be assumed that the person handling the radioactive material or the one responsible for accelerators, etc., knows how to protect himself, his co-workers, and his environment. An encouraging sign that university and hospital administrations are concerned on this score is the increasing number of requests for trained health physicists.

It might be of interest to this group to know where the AEC Fellows in Radiological Physics are finding employment. I have accurate information only on those who have trained at Oak Ridge National Laboratory and at Vanderbilt University-Oak Ridge National Laboratory (See Table I). At present 5 of these men are employed by universities; previously two other universities had Fellows on their staffs but lost them to the Army and to the AEC. I know that there are other schools who have trained health physicists on their staffs.

At the present time I have knowledge of seven universities which are seeking trained health physicists, an indication that schools are becoming increasingly aware of the need for someone to be responsible for radiation problems.

*(Para el sumario en español, véase la página siguiente.)*

## SUMARIO

## Educación y Adiestramiento de los Físicos Dedicados a la Higiene

La constante expansión de las obras de energía atómica, el creciente empleo de isótopos radioactivos y los problemas surgidos en la defensa pasiva y militar, en la higiene industrial y en el saneamiento del ambiente, han agudizado la necesidad de contar con físicos adiestrados en higiene. Estos varían del equivalente de los monitores de fábricas a los físicos radiológicos autorizados y muy bien preparados. En general, corresponden a tres clases: (1) el mero inspector, que ejecuta las tareas corrientes de higiene en las organizaciones

mayores que atienden a dicha rama en las obras de física; (2) el físico higiénico o superintendente subalterno que tiene a su cargo la vigilancia de la irradiación y los consejos sobre la misma en una esfera más elevada que la anterior; (3) el especialista o físico higiénico superior, sobre el cual recae en pleno la obligación de hacer cumplir los requisitos de protección contra la irradiación en un establecimiento o instalación grande. Bosquéjense aquí los requisitos correspondientes a cada una de esas categorías.

## DISCUSSION

**H. M. Parker, M.Sc.** (Richland, Wash.): I believe a discussant traditionally has four pleasures: the pleasures of (1) being asked to participate in the meeting, (2) being able to compliment the essayist on an excellent performance, (3) detecting a sin of commission in the paper, and brilliantly correcting it, (4) detecting a sin of omission, and rectifying it, usually at greater length than the original paper.

Your present discussant is essentially restricted to the first two of these pleasures. Those of us who are connected with Atomic Energy Commission operations in radiation protection are familiar with Dr. Anderson's outstanding personal contribution to teaching in this field. It has been good to get her views firsthand this morning.

In the matter of sins of commission, these are minor and perhaps contained in the opening phrase, "Health physics is a growing profession." There are those of us who believe that the health physicist is much like Santa Claus—he obviously does a great deal of good, but he doesn't really exist. This is largely a matter of terminology.

Sins of omission can be charged off to time limitations. We would like to see actual teaching schedules—perhaps these can be added in outline form in publication. Also, we would have liked to hear the essayist's views on the relationship of radiological physicists, as recognized by the American Board of Radiology, and of the apparently different radiological physics fellows of the AEC programs, to each other and to "qualified experts" as used by the National Committee on Radiation Protection.

I will close with a direct question: Have the

radiological physics fellows been made available first to universities, hospitals, and other institutions outside the AEC operations, where the immediate need is usually said to be greater?

**Dr. Anderson:** In answer to Mr. Parker's question: Yes, I believe they have been. The AEC in this program made a stipulation that these people have no responsibility to that organization after completing their training. Of course, we hope that, where AEC needs exist, they will be filled. I believe it is perhaps in part due to the fact that they are in close contact with an AEC installation that the larger number of these men are going into AEC jobs. Probably, also, the majority of the jobs are in the new installations. Our own program furnished Idaho Falls with several of their health physicists. So I think it is logical that the majority will go into AEC jobs.

I do believe, however, from the large number of requests from universities and hospitals for names of trained people that we are helping them also.

**Question:** Do you have as many applicants as you can take? If so, you can't do very much selecting, but if you have ten times more applicants than you can train, you can pick those with the qualifications that you stipulate in your paper.

**Dr. Anderson:** We generally have around 200 applicants for 40 fellowships.

**Question:** Would you hazard a guess of how many you have trained?

**Dr. Anderson:** It would be rather hard to guess, since Mr. Parker undoubtedly has some very good people with him, and we have many in our own installation. I would guess that we have



trained, say 59 or 60. Rochester and Brookhaven have trained about an equal number. So out of this AEC program you have probably 100, and out of our installation I would guess that we have 20 to 25 in that class. I don't know how many Dr. Parker has.

**Question:** Would you say, for instance, that those who have gone through the training are all qualified whether they graduated or not?

**Dr. Anderson:** Certainly from the comments that I hear from people who have taken our men, I believe that they do feel that they are well qualified. Ohio State, I certainly know, is very happy with their man, and I believe Illinois is, and others to whom I have talked.

**Question:** Do you consider one year training for a graduate essentially adequate?

**Dr. Anderson:** For junior health physicists, yes. I believe they would go into a university and/or a hospital or a small institute and do a very fine job.

**Robert R. Newell, M.D.** (San Francisco, Calif.): The health physicist is not very well named. I'd rather call him a hygienist. Radiologic physics and health physics are branches of science. Now the radiologic physicist practices the art of measurement, and therewith serves the radiologist. The health physicist practices the art of protecting people from radiation injury—that's hygiene, isn't it—the preservation of health. So both of these specialists are practitioners, as well as scientists, and they need not only a scientific education but also training in their field of practice. My point is that education is comparatively easy, but training is a hard job.

I'll draw you a picture (on the blackboard). This fine monument is Radiation Hygiene, the art of preserving health in spite of potential radiation hazards. This big block of granite on which the monument stands is its scientific foundation. Call it Health Physics, if you will; see that not only physics but also chemistry and biology are in it, but see that it is just science.



# Radiology in a Small Community<sup>1</sup>

EDW. D. GREENBERGER, M.D., F.A.C.R.

McAlester, Okla.

IT IS THE OBJECT of this paper to show that the practice of radiology in a small community is stimulating, satisfying, and profitable. It is particularly directed to the young radiologist who contemplates establishing himself in some large, overcrowded, highly competitive city because

ogist—the author—in this area, who has complete charge of radiology in the two hospitals and at the McAlester Clinic,<sup>2</sup> in addition to carrying on a private practice. All the diagnostic work done in McAlester is performed in these four separate x-ray departments. All x-ray irradiation

TABLE I: TOTAL NUMBER OF X-RAY EXAMINATIONS IN EACH OF FOUR X-RAY DEPARTMENTS IN McALESTER, OKLA., JUNE 1, 1951, TO JUNE 1, 1952

	Author's Office	McAlester Clinic	St. Mary's Hospital	General Hospital	Total
Bones					
Extremities	401	577	310	247	1,535
Skull	60	89	48	44	241
Spine	135	122	57	77	391
Chest	215	418	232	264	1,129
Upper Gastrointestinal Tract	255	267	129	96	747
Colon	59	110	64	43	276
Gallbladder	70	139	95	84	388
Cholangiograms	0		3	16	19
Genitourinary Tract	40	116	56	142	354
Pregnancy	43	44	25	13	125
"Acute Abdomen"	5	13	61	56	135
TOTAL	1,283	1,895	1,080	1,082	5,340

he feels that the opportunities for a stimulating practice in a small community are too limited. It is also directed to our radiological colleagues in the larger medical centers, who sometimes question the experience and opportunities for service available to the radiologist in the small community. It is, in short, a statistical report of the type and amount of work that has been available to the author in his community.

McAlester, in southeastern Oklahoma, is typical of many small towns in the Southwest. It boasts a population of 20,000, but its medical and hospital facilities serve over 125,000 people in the adjacent sparsely populated counties. There are 23 physicians in McAlester and 12 physicians in the counties which utilize its services. The two local hospitals have 60 beds each. There is but one radiol-

therapy is performed in the author's office.

From June 1, 1951, to June 1, 1952, 5,340 diagnostic x-ray examinations were made in McAlester. A total of 1,023 x-ray studies were made of the gastrointestinal tract, 747 by means of barium administered orally and 276 by barium enema. Gastrointestinal work has offered some difficulties in view of the fact that these studies are carried out in the four separate departments, and all are a part of the morning's work. Encephalography, myelography, and angiocardiology have not been performed, patients requiring such studies being referred to specialists in the larger cities nearby. All x-ray studies for acute abdominal conditions receive prompt interpretation, regardless of the time of day.

Table I outlines the amount and type of diagnostic roentgenology performed in each

<sup>1</sup> Accepted for publication in December 1952.

<sup>2</sup> In February 1953, the McAlester Clinic obtained the services of a full time radiologist.

of the four x-ray departments in McAlester under the author's supervision for the last fiscal year.

No attempt has been made to record the total number of superficial and deep x-ray and radium treatments administered in the past years. Nor is there a record of the

TABLE II: SKIN, LIP, AND MOUTH CANCERS TREATED FROM JUNE 1, 1951, TO JUNE 1, 1952

	Basal-Cell Carcinoma	Squamous- Cell Carcinoma	Total
Skin			
Cheeks, forehead, temple	32	20	52
Nose	18	13	31
Eye	5	1	6
Ear	2	4	6
Neck	5	10	15
Extremities		5	5
Lip	6	22	28
Mouth	1	8	9
TOTAL	69	83	152

number of patients treated for benign skin conditions, inflammatory lesions, lymphoid hyperplasia and lymphadenopathy, arthritic pain, herpes zoster, menopausal bleeding, etc. An attempt has been made, however, to keep an accurate count of all patients treated for malignant disease.

Skin carcinomas are the most prevalent form of malignant growth encountered in the Southwest. Since most patients travel many miles to receive x-ray therapy for skin carcinomas, rapid x-ray treatment has been adopted in most cases: 1,000 to 1,500 r of superficial x-ray irradiation on each treatment day for four to five treatments within a period of ten days. Fractional x-ray irradiation at medium or high voltage is given to those patients who have larger elevated lesions. For the past five years, radium has not been used for skin or lip cancers. Biopsy of all such lesions was performed in the author's office by means of the scalpel and electric knife. Table II is a tabulation of cancers of the skin, lip, and mouth treated for the past year. A total of 115 skin carcinomas received irradiation in this period.

Table III lists the general types of cancer and the number of such patients

TABLE III: GENERAL TYPES OF CANCER TREATED FROM JUNE 1, 1951, TO JUNE 1, 1952

Carcinoma of the Breast	12
Stage I	2
Stage II	8
Stage III	2
Carcinoma of the Cervix	16
Stage I	8
Stage II	4
Stage III	4
Carcinoma of the Fundus of the Uterus	4
Carcinoma of the Ovary	2
Leukemia	4
Lymphoma (Hodgkin's, Lymphosarcoma, etc.)	2
Carcinoma of Respiratory Tract	3
Larynx	1
Lung	2
Carcinoma of Genitourinary Tract	6
Bladder	2
Prostate	1
Penis	2
Testis (Seminoma)	1
Bone Tumors	8
Fibrous dysplasia	1
Fibrosarcoma	1
Metastatic tumors	6
Metastatic Nodes and Tumors (primary site undetermined)	3
Carcinoma of the Thyroid	1
Carcinoma of the Parotid Gland	1
Carcinoma of the Submaxillary Gland	1
Carcinoma of the Antrum	1
Carcinoma of the Rectum	1
Carcinoma of the Vulva	1
Retinoblastoma (in 11-year-old boy)	1
TOTAL	67

treated in the period, June 1, 1951, to June 1, 1952. A larger number of cases of carcinoma of the cervix were encountered in this period than in previous annual periods. Table IV lists the number of benign and malignant gynecological conditions that have received radium therapy in a twelve-year period, 1937 to 1952 (this

TABLE IV: TOTAL NUMBER OF GYNECOLOGICAL CONDITIONS REQUIRING RADIUM THERAPY TREATED IN A TWELVE-YEAR PERIOD

Carcinoma of the Cervix	104
Stage I	30
Stage II	36
Stage III	30
Stage IV	8
Carcinoma of the Fundus of the Uterus	22
Menopausal Bleeding (at and beyond the menopause)	149
Benign Bleeding in Young Females	15
TOTAL	290

statistical radium therapy record was interrupted by demands of military service from 1942 to late 1945).

From a small hospital in Hanover, N. H., Porter and Sycamore (1) recently reported

113 cases of carcinoma of the cervix treated from 1930 to 1944. In the records of the Department of Radiology of the University of Nebraska, Hunt (2) found a total of 121 cases of carcinoma of the cervix treated from 1937 to 1941, or an average of 24 cases per year. In his private practice at the Nebraska Methodist Hospital, in a thirteen-year period, he treated 69 cases, or about 5 per year. The material available in McAlester, averaging 9 cases per year, thus compares favorably with the figures for other small communities.

The radium therapy technic employed in carcinoma of the cervix is similar to that of the Curie Institute of Paris. Fifty milligrams of radium, consisting of 15 cells of 3.33 mg. each, are usually divided among three platinum capsules in tandem and applied for seventy-two hours; after a rest period of twenty-four hours, they are re-inserted in a colpostat for sixty to seventy-two hours. Roentgen irradiation either precedes or follows radium therapy, depending upon the individual case. The author has had the good fortune to assume complete responsibility of every carcinoma

of the cervix that he has treated, both in the application of the radium and in the after care.

#### SUMMARY

The tables presented in this paper indicate that there is ample, interesting, stimulating, and remunerative work available to a radiologist in a small community. In the town of McAlester, Okla., from June 1, 1951, to June 1, 1952, a total of 5,340 diagnostic x-ray examinations were made. There were treated in this period 115 skin cancers, 37 lip and mouth carcinomas, and 67 other types of carcinoma, a total of 219 malignant lesions. The proper care of this number of cases of malignant disease is a challenge to any radiologist in any community.

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#### SUMARIO

##### La Radiología en una Colectividad Pequeña

Prueba de que el ejercicio de la radiología en una colectividad pequeña resulta estimulante y provechoso la ofrece la carrera del A. en una población de 20,000 habitantes del Sudeste de Oklahoma.

Los dos hospitales locales, la Clínica McAlester y la práctica privada del A. abarcan unas 125,000 personas de la ciudad de McAlester y del territorio adyacente. El A. es el único radiólogo de la zona y tiene a su cargo todo el trabajo radiológico de los hospitales y la clínica.

Del 1° de junio de 1951 al 1° de junio de 1952, se verificó un total de 5,340 exámenes para diagnóstico. En ese mismo período de tiempo, se trató, además de una variedad de dolencias no malignas, a 115 cánceres cutáneos, 37 cánceres de los labios y la boca, y 67 carcinomas de otras clases, formando un total de 219 lesiones malignas. La asistencia adecuada de ese número de neoplasias malignas obliga a desplegar todos sus recursos a cualquier radiólogo en cualquier localidad.



## Teletherapy Design Problems<sup>1</sup>

MARSHALL BRUCER, M.D.

THE USE OF radium and x-rays for therapeutic purposes has a long and distinguished history. Radium and x-ray machines, although of proved value, have some irritating limitations. The most important of these, concerning the biological response of tissue to radiation, are not considered in this discussion. Others are inherent in the design of physical machinery, which in turn depends upon the source of radiation. With radioactive sources, it is not only possible but also practical to design machines which will respond to every legitimate demand of the radiotherapist.

It is very probable that teletherapy units can be made and maintained more economically than can x-ray machines. Especially for higher voltages, artificial radioactive sources are in competition with roentgen rays and radium, and the basic principle of teletherapy design should be to meet and to better the desirable features of the historical irradiation apparatus.

Radioactive sources have released us from the 1 curie per gram specific activity limitation of radium and from the cumbersome tubes and electrical connections of the x-ray generator. However, looming large among the advantages of radioisotope sources are very rigid limitations. There is a wide gulf between the theoretical and the practical in source production, and the designer of a practical teletherapy machine must select a set of fundamental requirements in order to choose the best from many possible radiation sources.

*Dosage Rate:* The rate of irradiation is one of the factors which will determine whether a given isotope is or is not adequate for teletherapy. This factor depends upon the decay scheme of the

isotope. Some isotopes deliver large amounts of radiation in a short time; some deliver very small amounts even over a long period. Dosage rates below 10 r/min. have been used to good advantage, but such slow rates increase patient handling problems and are economically undesirable. On the other hand, rates over 100 r/min. are probably unnecessary and wasteful. It would be costly to design a shutter device for very high energies delivered at so high a rate. With full acknowledgment that the question is debatable, it is possible to accept a figure of approximately 20 to 40 r/min. as satisfactory. A radioisotope source which cannot meet this requirement should be considered inadequate. Again, if conditions exist where delivery much greater than 100 r/min. is desirable at treatment distances beyond 50 cm., a radioisotope source will probably be impractical.

*Energy of Radiation:* The energy of radiation is another fundamental factor. Radioisotope sources can be made which deliver radiation ranging from very low-voltage x-rays to approximately 3-mev gamma rays. For experimental machines, any energy level is useful and monochromaticity is desirable. For practical therapeutic purposes, energy levels below a few hundred kilovolts are limited to superficial therapy, and it would be difficult for radioisotopes to compete with x-ray machines or with beta irradiators in this field. Above 200 kev, the marked difference in bone and soft-tissue absorption disappears; it may reappear above 7 mev (1, 2). Gamma energies from radioisotopes exist only up to about 3 mev. It is in this narrow hundred- to thousand-kilovolt range that radioisotopes enter

<sup>1</sup> From the Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

This is a summary of a more detailed discussion which has been circulated as an ORINS report, and it will be published as an AEC document through the Technical Information Service, U. S. Atomic Energy Commission, Oak Ridge, Tenn.

into consideration. If ultra-high voltages are necessary, radioisotope sources cannot be used.

Another factor to be considered in discussing energy levels is that of shielding and protection. In the kilovolt range photoelectric absorption allows the use of markedly less shielding, which is a structural advantage in building a machine. In the million-volt range, the somewhat increased dosage in depth of tissue may reduce the apparent advantage of kilovolt energies.

*The Source-Skin Distance (SSD):* The source-skin distance (SSD) is a fundamental factor affecting both source selection and machine design. Because the percentage depth dose increases with increased SSD, long distances are desirable. However, the inverse-square fall-off of radiation intensity causes a demand, at a long SSD, for a very high specific activity; this is costly. If low dosage rates are accepted, then treatment time is increased; this also is uneconomical.

A very short SSD has been used to advantage with some of the radium packs. There is, however, a scattered radiation from the ends of any collimating device which is of significant intensity with high-energy primary photons (3). Some, but not all, of the scattered radiation can be shielded out with properly designed filters. But at million-volt energies, it seems easier to leave a 10 to 15 cm. clearance between the skin and the end of the collimating tube. Because of the necessity for collimation, the restriction of penumbra and the mechanics of engineering, a shutter and diaphragming device, about 5 to 15 cm., is needed for the source-diaphragm distance. There is a minimum SSD, therefore, of approximately 15 to 50 cm. Below this distance all of the disadvantages of the radium packs become apparent. Radium has some very high-energy gamma emission to help overcome these disadvantages, which no other isotope can meet in competition.

While the minimum SSD is fixed by the penumbra and the engineering design, the

maximum SSD will be set by economic factors and a practical attainable specific activity. Large-diameter sources can be used if an accompanying long collimating distance is allowed. But specific activity must be very high to compensate for the inverse-square reduction in intensity. Adequate treatment intensity can be achieved with many isotopes at over 100 cm. SSD, but only at an uneconomical cost. It would appear that the distances available for consideration in teletherapy with radioisotope sources fall somewhere in the range of 30 to 100 cm. Distances from 50 to 90 cm. are probably practical limitations for large teletherapy machines.

*Radiation Protection:* The degree of personnel protection desired, the accuracy of collimation, and the energy of the source will determine the size of the machine. In the "off" position, in spite of shielding, there will always be some escaping radiation. The maximum shielding which can be desired is that which will allow one maximum permissible exposure (MPE)—6.25 mr/hr.—at the surface of the shield. With a recent history of demands for increased protection, this is the safest position to accept, though it is somewhat costly and unrealistic. The opposite extreme is the request for protection of such degree that a person working a few hours per day in the therapy room receives about 300 mr in one work week. Such a protection requirement may be legally precarious. It would be clumsy to administer without strict control, which seems equally costly and unrealistic. A compromise solution takes into account that actually only a small portion of personnel time is spent very close to the machine. A larger portion of time is spent at more than a meter distance. It is probable that the National Bureau of Standards *Handbook on Radium Protection* will be revised to include a statement that, in teletherapy machines, the shield shall be so constructed that at no point shall the radiation intensity exceed 6.25 mr/hr. at 50 cm. from the source in the "off" position and the construction shall be such that repairs and maintenance can be done at a

distance or with the protection of adequate additional shielding (4).

The protection requirements for diaphragms in both "off" and "on" positions have received much consideration in the design of x-ray machines. Although such recommendations are not routinely followed, the requirements of the National Bureau of Standards (*Handbook 41*) are reasonable (5). Protection requirements for the collimating device in the "off" position should be the same for the shield in any other direction. For permanently placed cones and diaphragms requirements should be the same as for the shield with the source in the "off" position. Adjustable beam-defining diaphragms with the source in the "on" position should probably follow the international recommendation, allowing transmission of not more than 2 per cent of the useful beam dosage rate outside the beam. With very little additional shielding, it is often possible to design collimating cones and diaphragms to reduce this transmission to less than 1 per cent.

*Single vs. Multiple Sources:* Teletherapy machines may be designed with a single large source collimated to produce a single beam of radiation or for multiple small sources collimated to converge at the lesion. The use of multiple small sources is a necessity where the specific activity is as low as that of radium.

In the use of multiple sources, both the angle of separation and the effective collimation of each source influence the shape of the area of most intense radiation. If there is a very narrow angle, there is an unacceptably narrow cone of radiation at the focal point, with a hot spot at the point closest to the source. If the effective collimation is reduced in a narrow-angle machine, the penumbra becomes very large and integral dosage becomes unacceptable. When the angle of separation is made very wide, the shape of the focal area is satisfactory, but the shielding around each source becomes so massive that such beam direction is better produced by multiple portals with a single beam than by multiple

beams from many sources. For these reasons, the use of multiple sources has been discarded in our thinking and emphasis has been placed upon the design of a single-beam machine which can be rotated to achieve the advantages of a multiple source unit.

All of the foregoing considerations must be taken into account in determining which isotopes can be put to practical use. To be a teletherapy source, a radioisotope must be available in relatively large quantities. It must afford a dosage rate better than the radium machines and equal to the commonly used x-ray machines. It must have a sufficiently long half-life to meet the competition of an x-ray tube. The energy of its gamma emission must be within a useful range for deep therapy, and it must have a specific activity which allows it to be used at desirable treatment distances. Its chemical composition must meet the requirements of packaging and loading.

#### ARTIFICIALLY PRODUCED RADIOACTIVE SOURCES AVAILABLE FOR TELETHERAPY UNITS

There may be a time in the future when the problem of availability of artificially produced radioactive isotopes will be only an economic matter to the radiotherapist. At the present time, high-flux reactor space is difficult to obtain, and the processing of fission products is still in its infancy. Immediate availability is thus foremost in considering any artificially produced radioactive isotope, though these problems are rapidly being solved.

There are six basic ways in which a radioisotope can be produced. The cyclotron was historically the first and still is the most flexible agent for this purpose, but it and other high-energy accelerators are formidable physical instruments. Production of a multicurie source by this means is not a matter to be considered lightly. Cyclotron-produced isotopes will be of little value to the practical radiotherapist for some time to come.

Another method is the separation and

purification of naturally occurring radioactive isotopes. Although not artificial radioactive sources, these are of historical importance and form a basis for comparison with the artificial isotopes. Of all the naturally occurring radioisotopes, radium and its decay products are the only practical sources for medical purposes. Radium has a specific activity of 1 curie/gram and is the base line from which all other isotopes must be judged. To be useful in a teletherapy machine, any isotope must have a higher specific activity than 1 curie/gram or a much higher radiation intensity than 8.4 r/hr. at 1 cm., or must be cheaper and more available than radium.

With the invention of the nuclear reactor, it became possible to produce large volumes of artificial radioisotopes. Three methods are available with neutrons; one is the use of fast neutrons. Fast neutron reactions involve expensive modification of the spacing and moderator in most existing reactors. Most of the  $C^{14}$  now available and the carrier-free  $P^{32}$  are produced by this method. However, the cross section for neutron-proton reactions is in many cases unknown, and the method is usually highly inefficient. It does not appear to be a practical means of producing multicurie sources of interest to the tele-therapist.

The chemical separation of daughter elements is a method for producing some isotopes. A thermal neutron reaction produces a short-lived isotope, which decays to a long-lived isotope separated chemically from its parent. None of the reactions of these types yield practical sources for tele-therapy machines.

The third method of neutron production is by the use of thermal neutrons to cause a neutron-gamma reaction. The most familiar example of this is  $Co^{60}$ . The parent isotope,  $Co^{59}$ , is put into the nuclear reactor and exposed to low-velocity or thermal neutrons. These neutrons diffuse into the cobalt and some of the cobalt atoms capture a neutron. With this capture, an unstable  $Co^{60}$  isotope is formed. Every

5.3 years, about 50 per cent of the unstable atoms so formed decay, with the emission of an electron and two gamma photons. With many unstable  $Co^{60}$  atoms packed into a small volume, the emitted gamma photons can be collimated to form a beam of useful radiation. Almost every isotope is subject to such a reaction; however, a number of factors influence the efficiency with which this reaction occurs.

The number of parent atoms in the target and the number of neutrons available for capture both enter into the equation which predicts the efficiency of the reaction. The number of neutrons crossing a square centimeter of surface area per second is called the neutron flux. The neutron flux of the Oak Ridge reactor is said to average  $5 \times 10^{11}$ . The Canadian reactor has a much higher flux. Some reactors have very high fluxes but very small volumes; others have large volumes but low flux. The greater the neutron flux the greater the number of reactions and, hence, the easier it is to produce the desired isotope. But this does not occur instantaneously. It takes time for neutrons to wander into the area of capture, and the build-up of reactions is related to the half-life of the isotope formed. The decay process starts immediately after production of an unstable group of atoms and there is a time in the production of any isotope when the number of atoms being formed is equal to the number decaying. Beyond this point, no matter how long the exposure to a neutron flux, there is always a constant number of radioactive nuclei present. This is called a saturation level and can be estimated for any isotope by the number of parent atoms present, the number of neutrons, and one other factor called the cross section.

Some isotopes have a great predilection for capturing neutrons. Others seem only rarely to react. If a known number of parent atoms is placed in a field of a known number of neutrons, the probability of capture can be measured. The events can be pictured as follows. A thermal neutron moves through a space partially



occupied by atoms. If the atoms are very large, there is a good probability of collision and capture. If they are very small, the probability is poor. Hence, the probability of capture can be measured in terms of a cross-sectional surface for each atom. Some atoms present a very large cross-sectional face to thermal neutrons, and hence have a cross section as high as  $10^{-20}$  sq. cm.; some are as low as  $10^{-32}$  sq. cm. Since nuclear dimensions are very small, instead of centimeters as the measure of size, a smaller unit has been chosen. The convenient unit,  $10^{-24}$  sq. cm., has been accepted as the measure of cross section and is called the "barn." Some parent isotopes have cross sections measured in terms of milli-barns. At least one parent isotope has a cross section as high as 180,000 barns. With a knowledge of cross section and the number of parent atoms and neutrons, we can calculate the curies of activity which can be produced for any radioisotope.

Many other factors enter into a definitive equation of thermal neutron production. Each atom transmuted also has a probability of capturing another neutron, and a double reaction or more may occur. While nuclear dimensions are very small, even the finest powders or the thinnest foils put into the reactor are very large. The outer surface of atoms will protect the inner atoms, and geometrical factors must be considered. Even minute contaminants might have high cross sections and preferentially capture and thus reduce the neutron flux in the immediate area. But the three factors mentioned are sufficient for calculating the relative expected yield and determining which isotopes are feasible from the standpoint of production by neutrons.

The final method of production of teletherapy sources is by the separation of fission products. In the process of maintaining a nuclear chain reaction, a constant flux of neutrons is maintained from the fission of uranium. While the neutrons and the energy released of each fissioning atom are used to produce power or to make

plutonium or to cause some other nuclear reaction, the fragments of the fission accumulate as a waste product. As they accumulate, they decrease the number of fissionable atoms present, they absorb neutrons themselves, and hence poison the reactor. For this reason, the slugs of fuel must periodically be removed from the reactor and refined to their original purity. The fission products thus removed are a host of elements from the middle of the periodic table. Most of these elements are radioactive and decay by beta and gamma emission to some stable element. Many decay very rapidly, but some decay with half-lives measured in terms of years. Ordinary chemical methods can be used to separate out each of the elements in pure form, except that the material is present in relatively small amounts dissolved in large volumes of fluid and is intensely radioactive.

The first problem in producing such sources is the separation of the fission products and purification without the addition of isotopic carrier so that a product of high specific activity is obtained. The chemical engineers who purify fission products must contend with the increased complexity of remote-control processing apparatus, the effects of intense radiation in materials, and the necessity for essentially foolproof operational technics. After preparation of the pure radioactive material, an entirely new set of problems is confronted in drying it, handling the dry solids, and fabricating a sealed source. Processes and technics for accomplishing this have been developed, but up to now such separations and purifications have not been made on the kilocurie scale required for teletherapy sources.

A good example of the complexity of the process is illustrated in the production of  $\text{Cs}^{137}$ . During the formation of this isotope, comparable quantities of other cesium isotopes are being produced in the same fission process, and some are stable. In chemically isolating  $\text{Cs}^{137}$ , the stable and other cesium isotopes are necessarily separated with it, thereby reducing the specific

activity of the material which can be obtained. In addition to the stable isotopic diluent, other elements such as rubidium and potassium, which have chemical properties very similar to cesium, are formed or are introduced from impurities in chemical reagents and other sources. There is also a practical limit to which such impurities as iron, lead, calcium, magnesium, and silica can be removed.

Since cesium is not chemically stable in pure form, it must be prepared in the form of a chemical compound, the radiation stability of which must be carefully considered. For example, nitrates of cesium would not be desirable because they decompose under intense radiation. Some compounds add too much weight and hence reduce the specific activity of the material. Thermal stability, hygroscopicity, decrepitation of crystals, all influence the choice of a compound. To approach true density of the chemical compound in the finished source, it is necessary to compress the material under high pressure. With such a long-lived source as  $\text{Cs}^{137}$ , there is by definition a slow decay rate; hence, there must be more material in a given source, and the source must therefore be larger, than for a short-lived radioisotope. It is evident that, although long half-life is convenient and point sources are desirable, some sacrifice must be made.

The mechanical operations in fabricating such intensely radioactive sources are a major problem. The cesium sulfate must be pressed into a thin inner container and sealed. Since each grain of material is highly radioactive, even minute contamination can be dangerous. After inspection and testing, the inner source must be sealed within the actual source holder. Since there is always the possibility of the build-up of gases within such sources, it is necessary to store them for several months so that they may be inspected for leakage, swelling, and other evidences of deterioration.

#### SELECTION OF AN ISOTOPE FOR A TELE THERAPY UNIT

Given a set of requirements for a teletherapy machine and a method for producing the source, it is desirable to see which isotopes appear to be practical possibilities. There are approximately 945 isotopes; 744 are either stable or have half-lives measured in terms of seconds to hours and are unadaptable to teletherapy. Probably the shortest half-life that could be considered as even remotely possible in teletherapy is approximately sixty days; only 99 such isotopes exist. Since cyclotron- and fast-neutron-produced isotopes are impractical at the present time, only the thermal neutron reaction and fission products can be considered. Many of these 99 have either no gamma radiation or an unknown or exceedingly weak gamma radiation and ought therefore to be discarded from the present discussion. Only about 37 isotopes have both a sufficiently long half-life and a significant gamma radiation to be considered. Thirty-five are produced in a reactor and two in fission.

In deciding which of these 37 are of practical value, it is necessary to know the specific activity available with each isotope. It would be far more useful to know the roentgens per hour output of a point source of each isotope, but in many cases the decay scheme is unknown and such a figure cannot be computed.

In the case of the thermal-neutron-produced isotopes, it is possible to calculate the number of curies which can be produced. If an infinitely thin sample of the pure element is put into a given flux of neutrons in perfect geometry then, for example, europium 152-154 would reach a saturation activity of  $4.9 \times 10^{12}$  disintegrations per second. The number of disintegrations per second at saturation activity ranges from  $10^{12}$  to  $10^6$  in the 35 isotopes produced by neutron reactions. A long series of calculations have made it fairly obvious that the use of enriched parent isotopes, an extremely expensive

TABLE I: RADIOISOTOPES WHICH MIGHT BE CONSIDERED FOR THERAPY SOURCES

Isotope	Half-Life	Gamma Energy (mev)	Practical Clinical Form	Production	Highest Practical Volume Specific Activity (curies/c.c.)**	Relative Radiation Intensity††
Radium 226	1620 yr.	0.2-2.2	Sulfate	Natural	5	1.0
Cesium 137	33 yr.	0.661	Sulfate	Fission	95	0.4
Europium 152-154	12.4 yr.	1.0*	Oxide	Thermal neutron	100	0.9
Cobalt 60	5.3 yr.	1.2†	Metal	Thermal neutron	275	1.6
Cesium 134	2.3 yr.	0.5-1.3	Sulfate	Thermal neutron	125	1.4
Cerium 144	275 days	0.06-2.6‡	Oxide	Fission	2000	0.2
Silver 110	270 days	0.6-1.5	Metal	Thermal neutron	250	1.5
Thulium 170	127 days	0.08	Oxide	Thermal neutron	550	<0.01
Tantalum 182	117 days	0.04-1.2	Metal	Thermal neutron	1500	0.7
Scandium 46	85 days	0.9-1.1	Oxide	Thermal neutron	500	1.3
Terbium 160	74 days	0.1-1.1	Chloride (?)	Thermal neutron	50	0.3
Iridium 192	70 days	0.1-0.6	Metal	Thermal neutron	975	0.4

\* Following filtration with 3.0 mm. of Pb, 83% of radiation is from four high energy protons averaging 1.08 mev (doubtful).

† Average of two protons at 1.17 and 1.33 mev.

‡ Gamma activity from 17 min. praseodymium daughter; energy levels are doubtful.

\*\* One year irradiation in  $5 \times 10^{14}$  n./cm.<sup>2</sup>/sec., one year removal from reactor, ideal geometry, for (Th-n,  $\gamma$ ).

†† Most of these figures are based on incomplete data and are highly unreliable.

procedure, does not significantly add to the desirability of any other elements.

Some complicating factors must be taken into account in calculating the production of isotopes by neutron reactions. The isotope cannot be used at saturation activity, since this would involve an irradiation time of four to six half-lives. Reactor space and time are extremely valuable, and it would probably be impractical to allow an irradiation period longer than approximately one year. Also, as each radioactive atom is formed, it is immediately liable to decay. During the period of irradiation and following removal from the neutron flux, the specific activity will change at a rate measured as the half-life. It will be found easier to discuss the relative desirability of various isotope sources if a decay period of, for example, twelve months following removal of the isotope from the reactor, is accepted as a standard figure.

Still another factor must be taken into account in deciding which isotopes are of value. The density of the material will determine how much can be placed in a given volume. Conversely, if it takes a given number of grams to produce a kilocurie source, then the volume per gram will

determine the amount of space taken up by the source. For the purpose of calculation and comparison with radium, a 1-c.c. source size was selected and the number of curies calculated either for the metal or, where this was impossible, for the salt of highest density. Radium under these circumstances would yield approximately 5 curies, and any other source of radioactivity must compete with this figure.

If then we accept an irradiation period of twelve months, a decay period of twelve months, a total volume of 1 c.c. irradiated under ideal conditions in a flux of  $5 \times 10^{13}$  neutrons/cm.<sup>2</sup>/sec., the isotopes listed in Table I can compete with radium. It is evident that only 11 isotopes remain of the original 945 which were considered. These are summarized in the table.

In spite of its very short half-life, the iridium isotope is very strong even after a year's decay. It has a somewhat lower energy but almost as wide a spectrum as europium. However, its 70-day half-life is a decided disadvantage and, since it has no advantage over an isotope such as europium, it can be dismissed as of secondary value in comparison with some of the longer lived isotopes.

A thulium source would be very strong

in curiage. However, only about 0.1 per cent of the disintegrations result in a gamma emission, and these are at 85 kev. Although the curiage is high, the rhm is very low. Thulium may be of value as an experimental source for biological investigation, but not for a teletherapy unit.

A tantalum source would have a spectrum of radiation as wide as europium but is far weaker and has a much shorter half-life. Since it offers no advantages and has many disadvantages compared to europium, it can be dismissed from the present discussion.

Cesium has by far the longest useful life of any of the artificially produced isotopes. Its highest practical volume specific activity does not approach some of the thermal-neutron-produced isotopes and it has a lower radiation intensity than radium.

Of the thermal-neutron-produced isotopes, europium and cobalt have the longest useful lives. Cobalt 60 has a higher radiation intensity than europium, and europium has a number of high cross-section daughter reactions which poison the build-up of specific activity. The effective energies of the two isotopes are about the same. The relative radiation intensity of europium per curie of activity is still unknown. Cobalt 60 has one feature, monochromaticity, not present in europium. However, with the filtration of approximately 17 per cent of its low-energy emission, europium is essentially monochromatic at a million volts.

#### SUMMARY

A review of the current status of the production of multicurie sources indicates that there are two outstanding isotopes which have a combination of advantages which make them suitable for teletherapy units: cesium 137, and cobalt 60. Cobalt 60 sources can be produced in specific activities ranging from 20 to 30 curies per gram. It is apparent that within the next

few years activities up to 100 curies per gram could be made available. Cobalt sources must be replaced every five to ten years. There is a significant change in output from year to year.

Cesium sources can be produced with specific activities not exceeding 23 curies per gram. It is a waste product in the neutron economy and, once the manufacturing plant is set up, it should be the cheapest of all sources. The source must be replaced from every thirty to fifty years. There is no significant change in output from year to year. However, cesium must be produced as a  $\text{Cs}_2\text{SO}_4$  salt and must be pressed into a sealed housing. Cesium sources can be housed in shields one-fourth as massive as an equal cobalt source.

Which of these sources can be considered "best" for the teletherapist is debatable. Only a long-range program, using each to its best advantage in the actual clinical practice of radiotherapy, will give a reasonable evaluation of these sources for teletherapy machines.

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## SUMARIO

## Problemas de Diseño en la Teleterapia

Un estudio del estado actual de la producción de focos de multicuries indica la existencia de dos isótopos destacados que poseen una combinación de cualidades que los capacitan para aparatos de teleterapia: el cesio 137, y el cobalto 60. Pueden producirse focos de cobalto 60 en actividades específicas que varían de 20 a 30 curies por gramo. Las fuentes de cobalto tienen que ser repuestas cada cinco a diez años, habiendo de año en año un cambio importante en la producción.

Pueden producirse focos de cesio con actividades específicas que no excedan de 23 curies por gramo. El cesio es un producto de desecho en la economía de los neutrones, y una vez instalado el establecimiento manufacturero, debe ser el más barato de

todos los focos. El foco no tiene que ser repuesto más que cada treinta a cincuenta años y no hay mayor cambio en la producción de año en año. Sin embargo, el cesio tiene que ser producido en forma de sal  $\text{Cs}_2\text{SO}_4$  y debe ser comprimido en un receptáculo sellado. Los focos de cesio pueden ser abrigados con resguardos cuatro veces menos macizos que los de un foco igual de cobalto.

Es dudoso cuál de esos focos puede considerarse como "mejor" para el teleterapeuta. Sólo un plan a largo plazo que utilice cada uno de ellos en su mejor forma en la real aplicación clínica de la radioterapia, proporcionará una justipreciación razonable de esos focos para los aparatos de teleterapia.

## DISCUSSION

(Papers by Braestrup, Green, and Snarr<sup>1</sup>; Failla<sup>2</sup>; and Brucer)

**Carl B. Braestrup** (New York, N. Y.): It is interesting to note that all three of these reports agree on the use of basically the same type of beam orientation, that is, converging beams from a spherical surface which defines the location of the source, or sources. Dr. Failla has succeeded in developing an effective radium irradiator. However, radium is less likely to be used for teletherapy in the future, due to its low specific activity, requiring a relative short treatment distance and use of multiple ports. The short source distance increases the volume dose, since the average path of the rays through the patient is longer. Furthermore, multiple-source irradiators lack flexibility and require more bulky shielding than a single source.

Dr. Brucer has indicated factors which should be considered in the selection of radioisotopes for teletherapy. At present Cobalt 60 and Cesium 137 have received the greatest attention. Of these Cobalt 60 has an advantage which should not be overlooked: that is, its greater energy and, as a result, a more effective dose distribution in the patient. Its 1.17- and 1.33-mev gamma rays correspond to about 3-million-volt x-rays, while with Cesium 137 the equivalent is about 1.5-million-volt x-rays.

The higher energy, of course, makes the shielding requirements higher for Cobalt 60 compared with Cesium 137. The difference, however, is not as great as might be expected, as the penetration of the scattered rays is essentially the same in both cases. A long half-life is obviously desirable. However, this becomes less important if the replacement of the source can be done with ease and insignificant exposure to the personnel involved. Mr. Green has developed one method which appears to have accomplished this.

**Robert Robbins, M.D.** (Philadelphia, Penna.): Our tentative decisions as to the type of high-energy therapy unit that we would like to own have been markedly modified by the demonstration of the unit designed by Mr. Green for Mr. Braestrup's installation. If one agrees that rotation therapy, the movement of either the patient or the beam, is a desirable way to treat tumors, then it seems to me that the mechanical aspects of performing this type of therapy are exploited to their fullest by the type of design presented today.

The possibility of feeding information to a computer type of device, resulting in highly individualized isodose patterns, is interesting. I can conceive of no other way in which all of the potentialities of this device could be useful. I

<sup>1</sup> Published in *Radiology* 61: 614-624, October 1953.

<sup>2</sup> To be published.

would hate to have to be the one to calculate manually the dose distribution from this type of apparatus.

I look with envy on the physicists who are able to have the satisfaction of proposing and solving a problem in this way, and wish that we in clinical therapy could solve our problems to the same satisfactory degree. Perhaps we should ask the physicists to turn their attention, at least partially, from the design of equipment to the problems of finding out where the tumors are and how big they are. It is not outside the realm of possibility that the type of approach and thinking we have seen today can help us to locate and define tumors and thereby make their radiotherapy even more adequate than at present.

**H. E. Johns, Ph.D.** (Saskatoon, Canada): My own justification for presuming to discuss these papers is the fact that we have had a rather conservative type of cobalt unit in operation in Saskatchewan for the last year. It is a 1,000-curie source and gives an output of about 30 r per minute at 80 cm. The unit is suspended from the ceiling, leaving the floor completely free. It has proved to be very practical. This does not, of

course, rule out the possibility of using many other arrangements and other isotopes.

I was very much interested in the paper given by Mr. Green on his rotation unit, and as a physicist I feel that it presents many problems of dosage calculation which could be very interesting. It may mean that radiotherapists will have to hire more physicists to do the work for them.

I was also much interested in some of the remarks of Dr. Brucer. Again, I do not think it is a question of cobalt or cesium or europium. I would say it is a question of trying all of them, as he suggested.

There is one reason for preferring cobalt in a unit of this kind, and that is the skin-saving effect. The dose on the surface of the skin in our unit is about 40 per cent of the dose at the maximum. The maximum dose occurs four to six millimeters below the surface of the skin. You may argue that this is no great advantage, but clinical experience to date shows that there is a very real skin-saving effect.

With cesium, the maximum dose would be about two millimeters below the surface. It is doubtful whether the skin-saving effect would be present with cesium.



## The Significance of Calcification in the Ascending Portion of the Aortic Arch

ABRAHAM WOLKIN, M.D.

IN THE GROSS pathologic specimen, the presence of arteriosclerosis of the aorta may give rise to confusion, masking a concomitant syphilitic aortitis (1). Radiologically, however, an accompanying arteriosclerosis with calcification makes demonstration of syphilitic involvement quite simple.

Uncomplicated syphilitic aortitis is characterized morphologically by little or no fatty deposition and no calcification (1). Its clinical recognition is extremely difficult or even impossible in the absence of demonstrable aneurysmal dilatation. A diffuse dilatation of the entire arch without localized aneurysm formation cannot be definitely distinguished from arteriosclerosis of the aorta (11). A delayed diastolic recoil and an increased systolic pulsation of the aorta which can be observed fluoroscopically have been described as characteristic of syphilitic involvement but only rarely have I been able to convince myself that I was witnessing this phenomenon.

Mallory states that calcification in the ascending portion of the aortic arch is unusual in arteriosclerosis unless the disease is far advanced (9). The earliest reference to calcification in association with syphilitic aortitis appears to have been made by Schatzki, who in 1942 stated that the presence of calcification is highly suggestive of that condition, particularly if the ascending aorta is involved, and that the presence of calcification proves rather than disproves the diagnosis (9). A rather high incidence of such calcification in the clinical material at this hospital and relevant reports in the literature (5, 12) stimulated the present study.

The material reviewed was observed

during the past four years. Most of the patients, therefore, are still alive. Eleven have died, and for 10 of these postmortem observations are available. All were found to have syphilitic aortitis with extensive arteriosclerosis and marked calcification.

A total of 95 cases diagnosed as syphilitic aortitis were reviewed, and in 54 of these calcification was found in the ascending portion of the aortic arch. As a control, the roentgenograms of 163 cases of arteriosclerosis of the aorta diagnosed during the same period of time but without serologic or other evidence of syphilis were reviewed. A total of 258 cases were thus studied.

The patients varied in age from fifty-one to seventy-seven years, averaging about sixty years. All were males, with a single exception (there was only one female ward in the hospital). The ratio of whites to Negroes was 4:1.

Of the 54 patients with calcification in the ascending aorta, 30 showed evidence of aneurysm formation, while in 24 there was no definite localized aneurysmal dilatation. Five patients had negative serologic findings and denied a chancre or other knowledge of syphilis. On further investigation, however, one was found to have been given 6,000,000 units of penicillin for "bad blood"; a second had a frank clinical aortic valve insufficiency with no history or other evidence of rheumatic heart disease; a third had unequal tendon reflexes and a bilateral positive Hoffmann's sign, and a fourth, fixed pupils. In neither of the latter 2 had the spinal fluid been examined. This leaves but one instance, in the present series of cases, of calcification in the ascending aortic arch that is not unequivocally syphilitic.

In 43 of the 54 patients, calcification was

<sup>1</sup> From Veterans Administration Center, Wadsworth, Kans. (Abraham Wolkin, M.D., Chief, Radiological Service). The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration. Accepted for publication in December 1952.

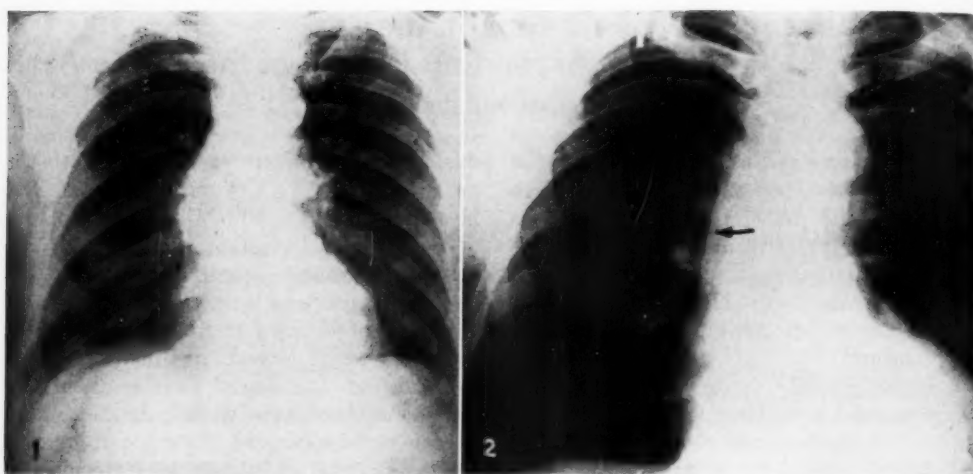


Fig. 1. Hilar density with marginal discontinuous linear calcification, identifying an aortic aneurysm.

Fig. 2. Linear calcification in the ascending aorta without dilatation. Syphilitic aortitis without aneurysm formation.

demonstrated also in the transverse and descending portions of the aortic arch; in 11 it was limited to the ascending arch. Thirty-two patients had x-ray evidence of cardiac enlargement. Of these, 8 had aortic valve insufficiency and the remaining 24 had arteriosclerotic or hypertensive heart disease or a combination of the two. In 3 of the 10 autopsied cases there was insufficiency of the aortic valve, and the remaining 7 showed coronary arteriosclerosis.

The predominant symptom was chest pain, and the second most common was shortness of breath. The average time elapsing between the initial chancre and the discovery of calcification in the aorta was about twenty years, with extremes of eleven years and forty years.

Previous reviews—notably those of Jackman and Lubert (5) and of Thorner and Carter (12)—have revealed substantially the same findings that are here reported except that the incidence of calcification in the ascending arch is higher in the present series. The fact that this group was made up of veterans, with repeated hospitalization and extensive therapy over a period of years, and that their treatment had perhaps in general been more intensive and prolonged than that of a comparable

civilian group, may be a factor in accounting for this difference.

The relationship of the syphilitic lesion to the arteriosclerotic changes has not been entirely clarified. It may be that, as a result of the inflammatory process in the ascending aorta, a superimposed degenerative change occurs (arteriosclerosis) at a site where this type of lesion is not ordinarily prominent. In other words, the calcification in the ascending aorta is arteriosclerotic—not primarily syphilitic, but rather a complication of syphilis (2, 3, 6).

It may be said that calcification, since it is a sign of late syphilis and indicative of infection that occurred years before, is of no great importance. It is important, however, to be able to demonstrate even late syphilitic aortitis for a number of reasons:

1. The prognosis is probably better with adequate treatment (10).
2. At the present time, when penicillin is often used with little or no restraint and with great promiscuity, the danger of a Herxheimer reaction with possible disastrous result is always present (8). Therefore, any sign which can put the clinician on guard is extremely valuable.
3. Since cardiovascular syphilis is



serologically positive in only about 70 to 85 per cent of cases (10), a sign which is apparently as reliable as ascending arch calcification will aid in clarifying some obscure cases of cardiovascular disease with negative serologic findings. It should be noted that syphilis is a relatively frequent



Fig. 3. Planigraphic study of the aorta, demonstrating calcification in the ascending portion of the arch. Syphilitic aortitis.

cause of sudden death from heart disease. In 300 cases of sudden cardiac death, Martland at autopsy found syphilitic involvement in 101 (7).

4. With the marked increase in the incidence of pulmonary carcinoma in recent years, any sign which aids in distinguishing mediastinal masses of various types becomes of great value. To be able to identify some of these obscure densities as aneurysms is of great aid in the further management of a case.

5. The observation of an atherosclerotic process at a relatively uncommon site, or at least in a markedly intensified form at such a site, because of a preceding or



Fig. 4. Calcification in the ascending, transverse, and descending portions of the aortic arch with no aneurysm formation. Extensive arteriosclerosis with complicating syphilitic aortitis. Most of the circumference of the aorta is involved.

accompanying inflammatory reaction, may be of some significance in the further elucidation of the entire problem of the pathogenesis and management of atherosclerosis.

Often on a routine postero-anterior roentgenogram the calcification may cast a faint or equivocal shadow, or possibly none at all. With proper technic, however, it can often be clearly demonstrated where it is not visible on the ordinary film. We are accustomed to using the following procedure when attempting to demonstrate possible calcification in the ascending aorta. An over-exposed film of the chest is made in the postero-anterior projection, without the Potter-Bucky diaphragm, since a rapid exposure is necessary in order to avoid blurring due to motion of the pulsating vessel. The film is made at a tube-object distance of  $3\frac{1}{2}$  feet with the other factors the same as for a standard 6-foot film. Exposures in the lateral and left anterior oblique projections are also made at  $3\frac{1}{2}$  feet instead of 6 feet. This

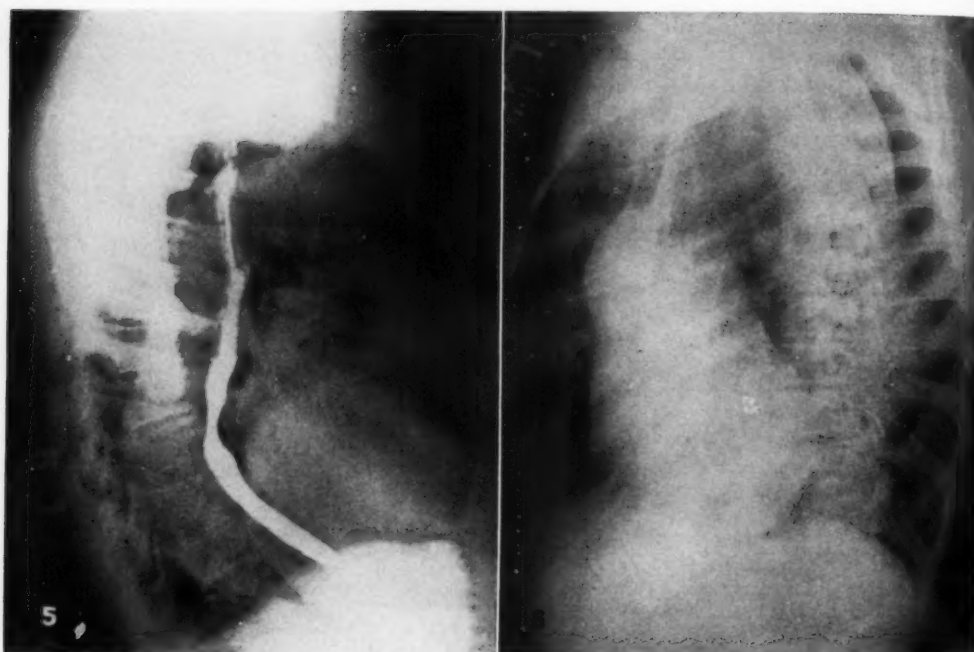


Fig. 5. Calcification in the ascending portion of the aortic arch, outlining diffuse aneurysmal widening due to syphilitic aortitis.

Fig. 6. Calcification in the ascending aortic arch, with fusiform type of aneurysm formation. Left anterior oblique projection.

affords marked improvement in contrast, and the mild exaggeration of the cardiovascular shadow is not disturbing. In every patient where there is any suggestion, either clinical or laboratory, that cardiovascular syphilis may be present, this procedure is followed. It has proved itself to be eminently worth-while in uncovering syphilitic aortitis that would otherwise go unrecognized. Another procedure which should prove useful, but with which we have had only little experience, is body-section roentgenography.

Misinterpretation of other densities as evidence of calcification must be guarded against. Mediastinal pleural calcification, rib calcification, projecting transverse processes, and the sternal margin are sometimes confusing, but careful film study will usually eliminate these sources of error. The pattern of calcification is quite characteristic, being linear and usually slightly discontinuous.

#### CONCLUSIONS

- (1) Calcification in the ascending aortic arch is a reliable sign of syphilitic aortitis.
- (2) A proper technic for its demonstration, easily carried out, is described.

NOTE: Grateful appreciation is tendered to Dr. Ira H. Lockwood, consultant in radiology, for his valuable advice and criticism in the preparation of this paper.

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## SUMARIO

## El Significado de la Calcificación en la Porción Ascendente del Cayado de la Aorta

La calcificación de la porción ascendente del cayado de la aorta constituye un signo fidedigno de aortitis sífilítica, habiéndolo observado el A. en 54 de 95 casos de dicha dolencia. Pasa por ser de origen arteriosclerótico, siendo una complicación más bien que una manifestación primaria de la infección sífilítica. Sugiere que, como consecuencia del proceso inflamatorio (sífilítico) en la aorta ascendente, se sobrepone una alteración degenerativa (arteriosclerótica) en un sitio en el que no suele destacarse esa clase de lesión.

Como la sífilis cardiovascular es con frecuencia negativa serológicamente, la calcificación de la porción ascendente del cayado

puede ayudar a esclarecer el diagnóstico en casos oscuros en otros sentidos.

Para descubrir la posible calcificación en la porción ascendente del cayado de la aorta, el A. toma una radiografía hiperepuesta del tórax en la proyección posteroanterior sin el diafragma de Potter-Bucky, dado que se necesita una exposición rápida para evitar la borrosidad debida al movimiento del vaso pulsátil. La radiografía se toma a una distancia tubo-objeto de 1.05 metros en vez de 1.8 metros. Esto facilita decidido mejoramiento en el contraste, sin que perturbe la leve exageración de la sombra cardiovascular.



# EDITORIAL

## Recommendations of the International Commission on Radiological Units

Revised at the Seventh International Congress of Radiology, Copenhagen, July 1953

### I. DEFINITIONS AND UNITS

1. *Intensity of radiation* is the energy flowing through unit area perpendicular to the beam per unit time. It is expressed in ergs per square centimeter per second or watts per square centimeter.

2. *Quantity of radiation* is the time integral of intensity. It is the total energy which has passed through unit area perpendicular to the beam and is expressed in ergs per square centimeter or watt-seconds per square centimeter.

3. *Absorbed dose* of any ionizing radiation is the amount of energy imparted to matter by ionizing particles per unit mass of irradiated material at the place of interest. It shall be expressed in *rads*.

4. The *rad* is the unit of absorbed dose and is 100 ergs per gram.

5. Inasmuch as calorimetric methods of determining absorbed dose are not usually practicable, ionization methods are generally employed. The quantity which must be measured is the ionization produced in a gas by the same flow of corpuscular radiation as exists in the material under consideration. The energy,  $E_m$ , imparted to unit mass of the material is then essentially related to the ionization per unit mass of gas,  $J_m$ , by the equation  $E_m = WsJ_m$  where  $W$  is the average energy expended by the ionizing particles per ion pair formed in the gas, and  $s$  is the ratio of the mass stopping power of the material to that of the gas.

6. Since the calculation of the absorbed dose from measurements of ioniza-

tion requires a knowledge of the parameters  $W$  and  $s$  as well as variables characterizing the radiation and the irradiated material, it is recommended that tables of the best available data be prepared and held under continual review.<sup>1</sup>

7. The roentgen (r) remains the unit of x- and  $\gamma$ -ray dose and its definition remains unchanged as below:

The *roentgen* shall be the quantity of x- or  $\gamma$ -radiation such that the associated corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign.

8. It becomes increasingly difficult to measure the dose in roentgens as the quantum energy of the x- or  $\gamma$ -radiation approaches very high values. The unit may, however, be used for most practical purposes for quantum energies up to 3 Mev.

9. *Integral absorbed dose* is the integration of the energy absorbed throughout a given region of interest. The unit is the *gram-rad*. 1 gram-rad = 100 ergs.

10. Amounts of radioactive material shall be expressed in curies. The accepted definition of the curie is:

The *curie* is a unit of radioactivity defined as the quantity of any radioactive nuclide in which the number of disintegrations per second is  $3.700 \times 10^{10}$ .

With this definition the curie is independent of the disintegration rate of radium.

11. It is suggested that the  $\gamma$ -ray emission be expressed in terms of roentgens per millicurie-hour at 1 cm. from a point source. This quantity is different for

<sup>1</sup> Preliminary reports on this subject were presented to the Commission and it is hoped will be published in the near future.



every isotope. Preliminary data have been compiled relating to a number of radioactive isotopes and will be supplemented from time to time.<sup>1</sup>

12. The ICRU requests the national standardizing laboratories to set up, interchange and compare standards of x-rays,  $\gamma$ -rays and radioactive isotopes, maintain close contact with each other, and generally by every means within their power further the improvement of methods of standardization.

## II. SPECIFICATION OF RADIATION TREATMENT

13. The specification of the conditions of radiation treatment should be such as to enable the treatment to be reproduced in all its essential features. The completeness of dose estimations, in roentgens or rads, will vary in practice, but all specifications should be as detailed as possible.

### A. *Beam therapy:*

(1) The nature of the beam may be conveniently characterized by stating the following factors:

- (i) The type of beam used, *e.g.*, x-rays, radium, cobalt-60, cesium-137, neutron, electron, etc.
- (ii) The peak voltage or the energy of the gamma radiation.
- (iii) The inherent and added filter.
- (iv) For x-rays the half-value layer in some material such as:  
Aluminum, 10 to 120 kv.  
Copper, 120 to 400 kv.  
Tin or lead, 400 kv. to 1 Mv.  
Lead, above 1 Mv.

(2) In the recording of technique and dosage the following considerations should be included:

- (i) The number, dimensions, and location of the ports of radiation.
- (ii) The source-to-skin distance.
- (iii) The time interval between successive treatments.
- (iv) The number of treatments given.
- (v) The total time over which a course of treatment is spread.
- (vi) The dose-rate at some suitable point and the time of each treatment.

(vii) Any two of the following factors should be recorded:

- (1) Air dose.
- (2) Backscatter factor.
- (3) Skin dose, for each irradiation.

For beam radiations with energies greater than 1 Mev and for rotation therapy other factors may be substituted.

(viii) The nature and method of use of "bolus" material.

(ix) Depth-dose values at appropriate points along the axis should be specified.

(x) Total tissue-dose determinations and calculations should be made as complete as possible.

At least the following total doses, in rads or roentgens, should be stated:

- (a) Maximum skin dose.
- (b) Maximum dose in irradiated tissue.
- (c) Maximum dose in tissue of interest or tumor.
- (d) Minimum dose in tissue of interest or tumor.

### B. *Surface, intracavitary, and interstitial use of radioactive substances:*

(1) The description of the treatment should be given in sufficient detail to permit duplication of the technique.

(2) The physical characteristics of the radioactive material should be given, including half-life and type and energy of radiations emitted.

(3) The nature and thickness of material traversed by the radiation before reaching the tissues should be stated.

(4) The amount of radioactive material in millicuries and the total millicurie-hours should be stated.

(5) The number of applications and spacing.

(6) The total time of the treatment.

(7) The total dose delivered to appropriate points of interest within the tissues.

### C. *Systemic treatment by radioactive isotopes:*

(1) The technic of administration

should be given in sufficient detail to permit duplication.

(2) The physical and chemical nature of the radioactive isotope should be stated, including half-life and type and energy of radiations emitted.

(3) The amount of radioactive material in millicuries should be stated.

(4) The effective half-life and the pattern of distribution in tissues of interest should be given as completely as possible.

### III. RULES GOVERNING THE SELECTION AND WORK OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL UNITS

14. (a) The International Commission on Radiological Units (ICRU) shall be composed of a Chairman and not more than twelve other members. The selection of members shall be made by the International Executive Committee (IEC) from a list of nominations submitted by the national delegations and by the ICRU itself. Members of the ICRU shall be chosen on the basis of their recognized activity in the field of radiological units and standards, without regard to nationality.

(b) The ICRU shall be composed of at least three medical radiologists and three physicists.

(c) The members of the ICRU shall be selected during one International Congress to serve through the succeeding Congress. Not less than two but not more than four members of the ICRU shall be changed at any one Congress. In the intervening period a vacancy caused by conditions beyond the control of the IEC shall be filled on the recommendation of the ICRU.

(d) In the event of a member of the ICRU being unable to attend the ICRU meetings, a substitute may be selected by the ICRU as a temporary replacement. Such a substitute member shall not have voting privileges at the meetings unless specifically authorized by the IEC.

(e) The ICRU shall be permitted to invite individuals to attend its meetings to give special technical advice. Such persons shall not have voting privileges, but

may ask permission to have their opinions recorded in the minutes.

15. The continuance of the records of the ICRU shall be in the hands of a secretary of the ICRU, elected by the ICRU from among its regular members and subject to the approval of the IEC.

16. The ICRU shall familiarize itself with progress in the whole field of radiation units and standards. The secretary shall be responsible for the preparation of a program to be submitted to the Commission for discussion at its meetings. Preliminary reports shall be prepared and circularized to all members of the ICRU and other specially qualified individuals at least six months before the meeting of the Congress.

17. The Chairman shall be elected by the ICRU during one International Congress to serve through the succeeding Congress. The choice shall not be limited to the country in which it is proposed to hold the succeeding Congress.

18. Decisions of the ICRU shall be decided by a majority vote, with the Chairman casting the deciding vote in a case of a tie. A minority opinion may be appended to the minutes of a meeting if so desired by any member and upon his submission of same in writing to the secretary.

### IV. SUBCOMMITTEES

19. The Commission has established two Subcommittees, on (1) x-ray standards, and (2) standards of radioactive isotopes.

#### MEMBERS OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL UNITS PREPARING THE ABOVE REPORT

H. M. Hansen, *Honorary Chairman*, Denmark

W. V. Mayneord, *Acting Chairman*, Great Britain

L. S. Taylor, *Secretary*, United States of America

A. Allisy, France

H. Holthausen, Germany

W. Binks, Great Britain	H. E. Johns, Canada	W. J. Oosterkamp, <i>Secretary</i> , Holland
R. H. Chamberlain, United States of America	W. J. Oosterkamp, Holland	A. Allisy, France
F. Ellis, Great Britain	B. Rajewsky, Germany	L. H. Gray, Great Britain
G. Failla, United States of America	R. Sievert, Sweden	H. Holthusen, Germany
PRESENT COMPOSITION OF THE ICRU		
L. S. Taylor, <i>Chairman</i> , United States of America	F. Ellis, Great Britain	H. E. Johns, Canada
	G. Failla, United States of America	B. Rajewsky, Germany
		R. Sievert, Sweden



## ANNOUNCEMENTS AND BOOK REVIEWS

### AMERICAN COLLEGE OF RADIOLOGY

The Annual Meeting and Membership Luncheon of the American College of Radiology will be held at the Drake Hotel, Chicago, on Feb. 5, 1954. The Fellowship Convocation and Annual Banquet will follow on the same day. On this latter occasion, by unanimous approval of the Chancellors, the 11th and 12th Gold Medals of the College will be awarded to Dr. Benjamin Orndorff, of Chicago, and Dr. W. H. Stewart, of New York, "for distinguished and extraordinary service to the American College of Radiology and to the profession for which it stands."

The Board of Chancellors of the College will meet on Feb. 3 and 4, and a meeting of the Councilors will be held at 2:00 P.M. on Feb. 4, followed by a dinner at 6:30.

The twenty-first Annual Conference of Teachers of Clinical Radiology is scheduled for Feb. 6, also at the Drake Hotel. The morning session, 9:30 to noon, and early afternoon session, 2 to 4:30, will be devoted to the subject, "The Future Evolution of Teaching in Radiologic Therapy."

The program will be opened by a discussion, Teaching the Radiologic Resident the Clinical Aspects of Cancer, by Douglas Quick, M.D., New York City. An outstanding pathologist will speak on The Training of Residents in Radiology in the Pathology of Tumors. Richard H. Chamberlain, M.D., Philadelphia, will present Training the Radiologic Resident in the Use of Isotopes.

The afternoon session will be introduced by a physicist discussing Training the Radiologic Resident in Radiation Protection. The final paper in this symposium will again feature a physicist, discussing, The Training of Physicists and Radiologists in Radiological Physics.

The remaining portion of the Conference will be devoted to a discussion of Hospital Accounting and Business Methods as they affect departments of radiology. Mr. Ronald Jydstrup, Advisor in Accounting with the American Hospital Association, has been invited to speak.

### KANSAS RADIOLOGISTS

The annual meeting of the Kansas Radiological Society and the Radiological Society of Greater Kansas City will be held at the University of Kansas Medical Center, Feb. 15-17, 1954. The guest speakers will be Dr. Earl Miller, University of California; Mr. Dale Trout, Physicist for the General Electric Company; Dr. John Caffey, Columbia University, New York; Dr. Harold Jacox, Columbia University, New York; Dr. Clyde Stevenson, Scott & White Clinic, Temple, Texas; Dr. Harry Weber, Mayo Clinic, Rochester, Minn.

Further information and a full program of the meeting may be obtained from G. M. Tice, M.D., University of Kansas Medical Center, Kansas City 3, Kansas.

### LOS ANGELES RADIOLOGICAL SOCIETY

The Sixth Annual Mid-Winter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Ambassador Hotel, Los Angeles, California, on Saturday and Sunday, Feb. 20 and 21, 1954. A banquet preceded by cocktails will be held at the Ambassador Hotel on Saturday evening, Feb. 20.

The out-of-state speakers will be Dr. Eugene P. Pendergrass, Philadelphia, Penna., Dr. U. V. Portmann, Tucson, Ariz., Dr. Marcy L. Sussman, Phoenix, Ariz., and Dr. Frederick E. Templeton, Seattle, Wash.

Conference reservations may be made through Doctor Harold P. Tompkins, 658 South Westlake Avenue, Los Angeles 57, Calif. The Conference fee is \$20.00, and the dinner will be \$7.50 per plate. Courtesy cards for the Conference are available to radiological residents and radiologists in military service, by preregistration.

Hotel reservations should be made as soon as possible through the Convention Manager, Ambassador Hotel, Los Angeles.

### MAINE RADIOLOGICAL SOCIETY

The following have been elected to office in the Maine Radiological Society for the year 1954. President, Dr. John D. Southworth, Togus; Vice-President, Dr. Clark Miller, Lewiston; Secretary-Treasurer, Dr. Jack Spencer, Maine General Hospital, Portland 4; Councilor, Dr. Forrest B. Ames, Bangor.

### SAN FRANCISCO RADIOLOGICAL SOCIETY

At a recent meeting of the San Francisco Radiological Society, Dr. Maurice Robinson was installed as President for the ensuing year. The following officers were elected: Dr. Charles S. Capp, President-elect; Dr. Ivan J. Miller, 2680 Ocean Avenue, San Francisco 27, Secretary-Treasurer; Dr. Joseph Levitin, Member of the Executive Board.

### INDIAN RADIOLOGICAL SOCIETY

Dr. N. G. Gadekar, M. B., B. S., D.M.R.E. (Camb.), Director of the Department of Radiology of Irwin Hospital, New Delhi, India, has been elected President of the Indian Radiological Society for 1954.

The Eighth Indian Congress of Radiology will be



held in Madras, Feb. 12-15, 1954. Any member of the Radiological Society of North America who may be in India at that time will be cordially welcomed. Further information concerning the meetings may be obtained from R. F. Sethna, General Secretary, Navasari Bldg., Hornby Road, Fort, Bombay 1.

#### SIXTH INTERNATIONAL CANCER CONGRESS

Physicians and scientists are invited to present papers at the VIth International Cancer Congress to be held in São Paulo, Brazil, on July 23 to 29, 1954, under the sponsorship of the International Union Against Cancer. The program will include sections on fundamental cancer research, on clinical studies on cancer, and on cancer control. Registration blanks are available from the Chairman, National Committee of the International Union Against Cancer, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C.

Detailed information regarding travel arrangements and hotel reservations may be obtained from Dr. Brewster S. Miller, American Cancer Society, Inc., 47 Beaver Street, New York 4, New York.

#### COURSES ON DISEASES OF THE CHEST

The Council on Postgraduate Medical Education of the American College of Chest Physicians, in cooperation with the respective state chapters of the College and the staffs and faculties of the local hospitals and medical schools, will sponsor the Second Regional Postgraduate Course on Diseases of the Chest, Feb. 15-19, 1954, in New Orleans, and the Seventh Annual Postgraduate Course on Diseases of the Chest, at the Bellevue-Stratford Hotel, Philadelphia, March 15-19, 1954. Tuition for each course is \$75.

Further information may be secured by writing to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

#### ATOMIC ENERGY COMMISSION FELLOWSHIPS

Applications for U. S. Atomic Energy Commission Fellowships in Radiological Physics and Industrial Hygiene for the 1954-55 school year are now being received by the Oak Ridge Institute of Nuclear Studies.

The Industrial Hygiene fellowship program supports a limited number of individuals who are studying for the master's degree in this field at the Harvard University School of Public Health and the University of Pittsburgh Graduate School of Public Health.

Radiological Physics fellowships are carried out in three separate programs as follows: At Vanderbilt University and Oak Ridge National Laboratory, at the University of Rochester and Brookhaven Na-

tional Laboratory, and at the University of Washington and Hanford Works. In each case, nine months of course work at the university is followed by three months of additional study and field training at the cooperating AEC installation.

The basic stipend for each fellowship is \$1,600, with additional family allowances.

Application forms and further information may be obtained from the Fellowship Office, University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

### Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

#### PLANNING GUIDE FOR RADIOLOGIC INSTALLATIONS.

By the Committee on Planning of Radiologic Installations of the Commission on Public Relations of the American College of Radiology, Wendell G. Scott, M.D., Chairman. A volume of 336 pages with 102 illustrations and 93 tables. Published by The Year Book Publishers, Inc., 200 E. Illinois St., Chicago, Ill., 1953. Price \$8.00.

#### THE YEAR BOOK OF RADIOLOGY (1953-1954 YEAR BOOK SERIES). RADIOLOGIC DIAGNOSIS, edited by JOHN FLOYD HOLT, M.D., Associate Professor, Department of Roentgenology, University of Michigan, and FRED JENNER HODGES, M.D., Professor and Chairman, Department of Roentgenology, University of Michigan. RADIATION THERAPY, edited by HAROLD W. JACOX, M.D., Professor of Radiology, College of Physicians and Surgeons, Columbia University; Chief, Radiation Therapy Division, Radiologic Service, Presbyterian Hospital, New York City, and VINCENT P. COLLINS, M.D., Professor and Chairman, Department of Radiology, Baylor University, College of Medicine; Radiologist-in-chief, Jefferson Davis Hospital, Houston, Texas. A volume of 462 pages with 399 figures. Published by The Year Book Publishers, Inc., 200 E. Illinois St., Chicago, Ill. Price \$8.00.

CLINICAL ROENTGENOLOGY. VOLUME I. DEVELOPMENTAL AND SYSTEMIC CONDITIONS AND LOCAL LESIONS IN THE EXTREMITIES. By ALFRED A. DE LORIMIER, M.D., Radiologist, Saint Francis Memorial Hospital, San Francisco, Calif.; Consultant in Radiology for the United States Army at the Letterman Army Hospital; Consultant in Radiation Therapy for the United States Public Health Service at the U. S. Marine Hospital, San Francisco, Calif.; Formerly, Commandant, the Army School of Roentgenology; HENRY G.

MOEHRING, M.D., Radiologist, Duluth Clinic, Duluth, Minn.; Formerly, Director, the Army School of Roentgenology; and JOHN R. HANNAN, M.D., Radiologist, Cleveland, Ohio; Radiologist, Lake County Memorial Hospital, Painesville, Ohio; Formerly, Director, the Army School of Roentgenology; Associate Professor, Diagnostic Roentgenology, the Frank E. Bunts Educational Institute, Cleveland Clinic Foundation; Staff, Department of Roentgenology, Cleveland Clinic Foundation. A volume of 492 pages, with 782 illustrations. Published by Charles C Thomas, Springfield, Ill., 1953. Price \$18.50.

RADIOACTIVITY AND RADIOACTIVE SUBSTANCES. By SIR JAMES CHADWICK, D.Sc., LL.D., F.R.S. With Foreword by Lord Rutherford, O.M., D.Sc., LL.D., F.R.S. Revised and Supplemented by PROF. J. ROTBLAT, M.A., Ph.D., D.Sc., F. Inst. P. A monograph of 120 pages with 41 illustrations and 12 tables. Published by Pitman Publishing Corporation, New York, 4th ed., 1953. Price \$3.00.

MENINGIOMAS OF THE POSTERIOR FOSSA. Acta Radiologica Supplement 104. By FRANCESCO CASTELLANO and GIOVANNI RUGGIERO. From the Neurosurgical Department (Director: Prof. Herbert Olivecrona) and the Roentgen Department (Director: Prof. Erik Lindgren), Serafimerlasarettet, Stockholm, Sweden. A monograph of 178 pages, with 129 illustrations. Published by Acta Radiologica, Stockholm 2, Sweden. Price Sw. Kr. 30:-

ARTERIO-EN AORTOGRAPHIE BIJ ARTERIËLE CIRCULATIESTOORNISSEN DER EXTREMITATEN. (ARTERIO-AND AORTOGRAPHY IN DISTURBANCES OF THE ARTERIAL CIRCULATION IN THE EXTREMITIES) with a summary in English, French and German. By DR. H. D. DE REUS, with Foreword by PROF. DR. R. H. DE WAARD, Hoogleraar in de Radiologie te Utrecht. A monograph of 190 pages, with 38 illustrations. Published by Drukkerij v/h Kemink en Zoon N.V., Utrecht, 1953.

STRAHLENSCHUTZ UND SONSTIGER ARBEITSSCHUTZ BEI DER MEDIZINISCHEN ANWENDUNG VON RÖNTGENSTRAHLEN. Die neuesten Unfallverhütungsvorschriften mit Erläuterungen. By DR. WILHELM ERNST, Leitender Technischer Aufsichtsbeamter und Röntgensachverständiger der Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege, Hamburg. A monograph of 97 pages with 22 illustrations. Published by Georg Thieme, Stuttgart, 1953. Agents for U.S.A., Grune & Stratton, Inc., New York, N.Y. Price DM 7.80.

OBENCÁ NEURORADIOLOGIE. By DR. JAN JIROUT. A monograph of 276 pages, with 214 illustrations,

and a supplement containing 347 roentgenograms with accompanying drawings. Published by Státní Zdravotnické Nakladatelství, Prague, Czechoslovakia, 1953. Price Kčs 78.

L'ŒSOPHAGE EN CARDIOLOGIE. ÉTUDE RADIOLOGIQUE DE L'ŒSOPHAGE DANS LES CARDIOPATHIES CONGÉNITALES ET ACQUISES. By MARCEL SEGERS, Chargé de Cours à l'Université de Bruxelles, and MARCEL BROMBART, Chef du Service de Radiodiagnostic à la clinique C. de Paep. Preface by Pr. Ch. LAUBRY. A monograph of 200 pages, with 135 illustrations. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris (VI<sup>e</sup>), 1953. Price 1,248 fr.

GRENZEN DES NORMALEN UND ANFÄNGE DES PATHOLOGISCHEN IM RÖNTGENBILDE DES SKELLETES (DR. A. KÖHLER). Ninth edition, fully revised by Dozent DR. E. A. ZIMMER, Bern/Fribourg. A volume of 672 pages with 1,282 illustrations. Published by Georg Thieme, Stuttgart, 1953. Agents for U.S.A., Grune & Stratton, Inc., New York, N.Y. Price DM 88.-

## Book Reviews

ROENTGEN-DIAGNOSTICS. By H. R. SCHINZ, W. E. BAENSCH, E. FRIEDL, and E. UEHLINGER. First American Edition (Based on the Fifth German Edition). English translation arranged and edited by JAMES T. CASE, M.D., D.M.R.E. (Camb.), Professor of Radiology Emeritus, Northwestern University Medical School, Chicago; Consultant in Radiology to the U. S. Marine and Passavant Memorial Hospitals, Chicago; Director, Memorial Cancer Foundation of Santa Barbara; Radiologist (Therapy), Santa Barbara Cottage Hospital, Santa Barbara, Calif. Volume III, Thorax. A volume of 1,116 pages with 1,085 figures. Published by Grune & Stratton, New York. Price \$45.00.

The long awaited Volume III of the English translation of Roentgen Diagnostics by Schinz *et al* is now available. This volume is a part of a projected series of five volumes under the supervision of Dr. James T. Case and his collaborators, who have again produced an outstanding work.

Volume III is devoted entirely to diseases of the chest. The bulk of the material has to do with the lungs, but the last 300 pages are concerned with changes in the cardiovascular system, including congenital heart disease. In the opening section of the work, on The Normal Chest, the technic of the roentgen examination and the anatomy and physiology of the lungs are covered. The second and much larger section, on The Pathologic Chest, occupies the larger portion of the volume. The coverage is unusually complete, including chapters on diseases

of the mediastinum and diaphragm. The last portion of the volume is devoted to diseases of the heart and blood vessels, with chapters describing the various congenital anomalies.

This work follows the best tradition of radiologic studies. It is well illustrated with pertinent radiographs and line drawings. A profuse bibliography of radiologic references is appended to each chapter. An index is included at the end of the volume.

Radiologists and clinicians interested in diseases of the chest will profit greatly by having this authoritative work available in English.

**THE RADIOLOGY OF BONES AND JOINTS. AN INTRODUCTION TO THE STUDY OF TUMORS AND OTHER DISEASES OF BONE.** By JAMES F. BRAILSFORD, M.D., Ph.D., F.R.C.P., F.I.C.S. (Hon.), Hunterian Professor, Royal College of Surgeons, England, 1934-35, 1943-44; Founder and First President of the British Association of Radiologists (now the Faculty of Radiologists); Emeritus Director of Radiological Studies in Living Anatomy, the University of Birmingham; Consulting Radiologist to the Queen Elizabeth Hospital, Birmingham, the Royal Orthopaedic Hospital, the Accident Hospital and the Warwickshire Orthopaedic Hospital, and other hospitals of the City; Active Fellow, British Orthopaedic Association; Awarded the Robert Jones Gold Medal and Prize of the British Orthopaedic Association, 1927, the Roentgen Prize, 1936, Encomienda Order Civil de Sanidad, Spanish Government, 1st Dallas B. Phemister Memorial Lectureship, University of Chicago, Hon. Socio Academia of Surgery, Madrid; Hon. Member University of Bordeaux; Hon. Member Roentgen Societies of Chicago, Detroit, New York, and Texas. Fifth Edition, with over 725 illustrations and 875 pages. Published by the Williams & Wilkins Co., Baltimore, Md., 1953. Price \$19.00.

Brailsford's text on the Radiology of the Bones and Joints has long been considered the most comprehensive work in the English language dealing with this subject. In the Fifth Edition, the author has thoroughly revised the subject matter and has added nearly 200 new illustrations and more than 100 pages.

The previous plan of presentation has been retained. Part I deals with regional anatomic studies, and Part 2 with disease processes which have a more widespread distribution. This arrangement has both advantages and disadvantages. In some instances it tends to separate too widely the available information on a given subject.

The illustrations are well chosen and in general show an improvement over those in previous editions. The paper is of excellent quality and contributes to good detail in their reproduction. A bibliography from the world literature is helpful. It would have

added value if the titles were given in all cases, as is done for the author's own works.

The book is nicely bound. The printing is good, but the single column format is less conducive to easy reading than the familiar two columns. This volume will have a well deserved place in the library of those interested in the skeletal system and its lesions.

**L'UROKYMOGRAPHIE ET LA RADIOMANOMÉTRIE URINAIRE.** By W. GREGOIR, Adjoint au Service d'Urologie de l'Université Libre de Bruxelles. A monograph of 226 pages, with 54 illustrations. Published by Masson et Cie, Éditeurs. Libraires de l'Académie de Médecine, 120, Boulevard Saint-Germain, Paris (VI<sup>e</sup>), 1953. Price 2,250 fr.

Following Stumpf's discovery of roentgen kymography in 1928, this method was used in studying numerous organs, including the upper urinary tract. Up to the present, however, these latter studies have been largely confined to research on development and physiology. The author hopes to apply kymography to the clinical study of patients with urinary tract disease. The following summary indicates the scope of the present study.

Among 800 urokymographic studies, 82 cases with dynamic alteration of the upper urinary tract were found, and 33 cases of the same nature were submitted to conservative surgical measures.

The multiple slit kymograph with moving grill is preferable to the multiple slit fixed grill, moving film method, since the picture more nearly approaches the usual urographic image. Usually 2 c.c. of 50 per cent Diodone are injected when retrograde pyelography is done. The first film is made thirty to sixty seconds after injection and retraction of the ureteral catheter. A second film is made one minute later. Further films may be taken, though it is to be remembered that the normal renal pelvis is evacuated in ten to fifteen minutes, sometimes sooner. In the usual intravenous urogram, maximal concentration of opaque medium in the renal pelvis occurs eight to twelve minutes after injection of 15 grams of contrast agent. This time is prolonged in the hydronephrotic kidney. Usually a kymogram is taken ten minutes after injection, before abdominal compression is applied.

Manometry of the renal pelvis is utilized when the patient has a nephrostomy, with the view of establishing the permeability of the upper urinary passage. The apparatus is similar to biliary manometric apparatus in current use. A separate manometer is connected with the bladder to obtain manometric zero with fluid in the bladder. The patient ingests no liquid for eighteen hours preceding the examination. A controlled debit of 5 c.c. per minute is allowed to flow into the renal pelvis, and manometric readings are taken every two to five minutes. The resultant curve will indicate normal ureteric flow, or partial or total obstruction. Vesical manom.

etry may be accomplished with a similar Y-tube arrangement to study the effect of renal pelvic pressure on vesical pressure, or to study the pressure in case of vesico-ureteral reflux.

Radiomanometry requires the use of radiopaque contrast material, 30 per cent Diodone being used. Barium may be used in vesical radiomanometry unless vesical diverticula are present. Use of the opaque substance allows correlation of pressure and radiographic findings. In dilated renal pelves an initial injection of 5 to 10 per cent contrast medium is made for filling the structure and the controlled debit is then instituted.

Urokiymographic manometry indicates completion of the manometric technic with a series of urokiymograms.

Speed and rhythmicity of ureteral contraction are recorded on the urokiymogram. Usually there are one to six contractions per minute and the speed of propagation is 2 to 6 cm. per second. The average diastolic phase of contraction is normally two seconds, twice as long as the systolic phase. Disturbances in conduction, antiperistalsis, and akinesia may be demonstrated. If the upper urinary tract is dilated and submitted to a permanent hyperpressure, a particularly rare phenomenon may be seen, which is called the "pendulary movement." After nephrectomy, the existence of antiperistaltism is spontaneous in the remaining ureter. The same phenomenon exists in some cases of obstruction or irritation of the lower ureter.

Many clinical observations may be made. Retrograde kymography records the presence of intermittent spasm at the ureteropelvic junction. In hydronephrosis it has been shown that the small renal pelvis may be akinetic, whereas certain megalo-ureters may retain excellent ability to contract. Knowledge of pyeloureteric function may be of value in planning and following surgical procedures. When possible, it is advisable to maintain muscular continuity by means of ureterotomy rather than by extensive plastic procedures. Uretero-intestinal anastomosis may be more successful if good peristalsis is present; if not, uretero-cutaneous anastomosis is preferable. Urokiymography should add to the knowledge of ureteral physiology in pregnancy.

A radiographic atlas of urokiymograms is appended, illustrating 54 observations in various physiologic and pathologic states.

This monograph illustrates an interesting dynamic approach to add to the usual morphologic studies of urinary tract disease.

**ATLAS D'HYSTEROGRAPHIE.** By P. BROcq, Professeur à la Faculté de Médecine de Paris; Chirurgien de l'Hôtel-Dieu; P. MOULONGUET-DOLÉRI, Professeur à la Faculté de Médecine de Paris, Chirurgien de l'Hôpital Tenon; R. MARICOT, Attaché de Gynécologie à la Clinique Chirurgicale de l'Hôtel-Dieu; and H. HARTMANN, Attaché de Consultation de Gynécologie à l'Hôpital

Tenon. A monograph of 104 pages with 140 figures. Published by Masson et Cie, Éditeurs. Libraries de l'Académie de Médecine, 120, Boulevard Saint-Germain, Paris (VI<sup>e</sup>), 1953. Price 1,440 fr.

For twenty years Brocq and his associates have correlated anatomopathologic specimens with hystero-grams. They have recorded their observations in this monograph. It is their belief that valuable information may be obtained by hystero-graphy. Genital infections, gross hemorrhage and possible pregnancy contraindicate use of the method.

Examples of normal, infantile, senile, and atonic uteri are shown by selected roentgenograms. The ante-flexed uterus may not fill, thus simulating the picture of aphasia. After correcting the position of the uterus, the hystero-gram may be normal. Examples of lateral deviation and retroversion are also shown.

Anomalies such as bicornuate and double uterus and absence of the vagina are illustrated. The findings in tuberculous peritonitis may give a bicornuate appearance to the uterus, but the outline is not smooth, as in the anomaly. Although hystero-graphy is in general contraindicated in the pregnant woman, it may be done in some cases in which the obstetrician is not certain that pregnancy exists. A retained placenta may be demonstrated, but considerable amounts of opaque medium may be expelled from the tubes into the peritoneal cavity during the first few days of the postpartum period. A dead fetus in the early months of gestation may be demonstrated.

Uterine myomas, polyps, endometrial hyperplasia, and carcinoma of the uterus are discussed and illustrated in successive chapters. Carcinoma is distinguished by the irregularity of the filling defect. Displacements of the uterus may be produced by extrinsic tumor. Endometriosis, sarcoma, tuberculosis, and endometrial adhesions following curettage are among the less common lesions seen.

Occasionally the veins or lymphatics draining the uterus are demonstrated, and sometimes rather large amounts of opaque medium spill into the peritoneal cavity. These incidents may be the result of the pathologic changes present.

This small atlas is easy to read and to understand, and the majority of lesions which one might expect in the uterus are clearly demonstrated.

**BRONCHIAALBOOM, SEGMENTEN EN BLOEDVATEN VAN DE LONG MET HUN VARIATIES.** The Bronchial Tree, the Pulmonary Segments, The Pulmonary Vessels and Their Variations. (With summary in English, French, and German). By FRITS KAREL and OTTO FRODL. Drukkerij en Uitgevers-Maatschappij v/h Kemink en Zoon N. V., Domplein 2, Utrecht, 1953.

Illustrated entirely by diagrammatic drawings, this small book, written largely in the Dutch lan-



guage, gives a good summary of the distribution of the bronchi, their nomenclature, and the pulmonary segments supplied by them. In addition, the relationship of the bronchi to the various pulmonary vessels and the distributions and variations of the latter are described. While the explanatory text is in Dutch, the summaries are in English, French and German, and the description of the diagrammatic illustrations is likewise in these three languages, so that the author's data are available to the reader of English. A final summary in these various languages is also given.

The nomenclature recommended by the International Congress of Otorhinolaryngology is used but the division into sub-segments follows that of Boyden and his associates, in so far as the bronchial tree is concerned. Gross anomalies of the bronchi and of the pulmonary blood vessels are not treated in this book. It does, however, give a good description of the usual variations in the bronchi and in the arteries and veins, with an attempt at a description of the pattern of such variations.

**LE OSSIFICAZIONI E LE CALCIFICAZIONI PACHIMENINGEE RETROSELLARI** (Quadro radiologico, reperto anatomico, criteri interpretativi). By G. LISCHI, Aiuto, and A. NERLI, Assistente, Istituto di Radiologia e Terapia Fisica dell'Università di Pisa (Direttore: Prof. Luigi Duranti). A monograph of 76 pages with 42 illustrations. Edizioni Minerva Medica, Torino, 1953.

This work deals with the radiologic picture, anatomic findings, and interpretation of those ossifications and calcifications found in the dura mater posterior to the sella. Lateral roentgenograms of the skull were made postmortem on 58 patients, and in 18 retrosellar opacities were demonstrated. The retrosellar area of the dura in the latter cases was removed intact, fixed, and studied histologically, together with the sphenoid sinuses. These studies showed that the opacities might represent amorphous deposits of calcium salts, true ossification, or a combination of the two. The formations were found either in the dura investing the clivus (parallel to this structure) or in the clinopetrous fold of dura. In the latter event they diverge from the sella as they proceed dorso-caudad. The ossifications are irregular heterogeneous streaks, or rounded or fusiform nodules. Calcification alone presents fine, homogeneous streaks. Another retrosellar opacity discussed is the osteophyte; this resembles opacities seen elsewhere, and is continuous with the cortex of a given bony structure. Most of the retrosellar osteocalcifications (other than the osteophytes) were associated with lesions of the dura, such as an obliterating endarteritis with plasma-cell and lymphocytic infiltration compatible with a syphilitic origin or a "reaction of adjacency" to a chronic sphenoid sinusitis. In some cases there was evidence of chronic inflammation with a histiocytic reaction of undetermined cause; in others, the

osteocalcifications were attributed to the involutional process of aging; in a few there were no significant histopathologic changes.

**LE GASTRITI (STUDIO RADIOLOGICO)**. By GIOVANNI GARDELLA and GIOVANNI SANQUIRICO, Istituto di Radiologia dell'Università di Genova (Direttore: Prof. A. Vallebona). A monograph of 114 pages, with 52 figures. Published by Licinio Cappelli, Bologna, 1952.

This monograph is intended to present the radiographic aspects of gastritis in its various forms, with some reference to its clinical and pathologic aspects as well. It begins with a discussion of the normal anatomy of the stomach, both gross and microscopic, with special emphasis on its mucosal aspects. This is followed by a discussion of the roentgen anatomy, with remarks on the technical aspects of the radiologic study of the mucosa. The authors favor Vallebona's "combined method" of mucosal study by means of a barium suspension and gas generated from the interaction of tartaric acid and sodium bicarbonate, and partial filling of the stomach, with pressure studies.

The work then takes up the various types of gastritis, beginning with the acute form, demonstrated by several roentgenograms showing the appearances of the stomach following ingestion of sulfuric and hydrochloric acid. The chronic variety, including the atrophic and hypertrophic, is subdivided into several groups. Illustrations of these groups are given. Purported examples of gastric syphilis and tuberculosis are presented. The differing points of view of the French and the German schools concerning the relation of gastritis to ulcer and cancer are discussed, the former believing that ulcer and cancer lead to gastritis and the latter that gastritis leads to ulcer and cancer.

As would be expected in a work dealing with such a controversial subject, many statements are open to question. However, a useful function has been accomplished, we believe, in counterbalancing the feeling in many American quarters that the roentgenologic examination has little or no part in the diagnosis of gastritis. As the authors point out, the fundus and the antrum are often difficult for the gastroscopist to visualize, and these are just the sites of predilection for gastritis. This reviewer certainly does not have the same degree of confidence in his ability to differentiate these antral and fundal gastritides from neoplasm as the authors. Even they admit that at times this problem cannot be solved by radiologic methods.

The authors mention that the roentgenologic examination will detect abnormalities that might elude the surgeon both with palpation and even direct inspection. Further evidence that the surgeon is not always the final arbiter between the radiologist and himself in gastrointestinal diagnosis can be found in a recent article by Rappaport (Ann. Int. Med. 39: 747, October 1953).

**ATOMIC MEDICINE.** Edited by CHARLES F. BEHRENS, M.D., Rear Admiral, MC, U. S. Navy, Staff Medical Officer, Eastern Sea Frontier; formerly Director, Atomic Defense Division, Bureau of Medicine and Surgery, Navy Department and Commanding Officer, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. A volume of 632 pages, with numerous illustrations. Published by the Williams & Wilkins Co., Baltimore, Md. Second edition, 1953. Price \$11.00.

The first edition of *Atomic Medicine*, published in 1949, is now followed by a second, bringing the reader up to date in this rapidly developing field. The text of the new edition follows closely the title, for while several of the early chapters are devoted to the physics of the atom and the atomic bomb, these take up relatively little space, serving as a background for the more extensive discussion of atomic energy in its disease-producing, diagnostic, and therapeutic aspects.

The twenty-two chapters, the work of twenty contributors, are supplemented by three Appendixes, including a useful table of isotopes and a listing of the symbols and definitions that have found their way into the medical literature with the growth of this new field.

Following the preliminary chapters on physics, there are discussions on subjects relating to the hazards involved in radiation and the protective measures which these demand. One chapter describes the pathological anatomy of total body radiation, others take up the fundamental biology, hematology, and permissible dosage. The latter half

of the text is devoted to radioactive isotopes and their uses in diagnosis and therapy. A chapter on the design and operation of radioisotope laboratories especially for research purposes offers practical suggestions as to design and equipment. A bibliography of pertinent references is given at the end of each chapter.

Those interested in ionizing radiation, and radioisotopes in particular, will find in this work a wealth of information.

**SYMPOSIUM ON CHROMOSOME BREAKAGE** (held at the John Innes Horticultural Institution, June 9-11, 1952). Supplement to *Heredity*, Volume 6. A volume of 315 pages, with numerous illustrations. Published by Charles C Thomas, Springfield, Ill., 1953. Price \$7.50.

This *Symposium on Chromosome Breakage* is not only of special interest to cytologists and geneticists but also of interest to radiologists, inasmuch as ionizing radiation is one of the potent means of producing chromosome breaks. Quite possibly these chromosome breaks play a significant part in the after-effects of radiation and may have some bearing on the genesis of post-irradiation cancer. As the title implies, this book is a series of papers on various aspects of the subject. The first ninety pages are devoted to radiation breakage, the next group to chemical breakage of chromosomes, and the latter part to spontaneous breakage and general considerations. The chief interest of the book to radiologists will be in the first portion. A useful comparison is provided by Revell of chromosome breakage produced by x-rays and by radiomimetic substances.



## RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

*Editor's Note:* Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

**RADIOLOGICAL SOCIETY OF NORTH AMERICA.** *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

**AMERICAN RADIUM SOCIETY.** *Secretary*, Robert E. Fricke, M.D., Mayo Clinic, Rochester, Minn.

**AMERICAN ROENTGEN RAY SOCIETY.** *Secretary*, Barton R. Young, M.D., Germantown Hospital, Philadelphia 44, Penna.

**AMERICAN COLLEGE OF RADIOLOGY.** *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

**SECTION ON RADIOLOGY, A. M. A.** *Secretary*, Paul C. Hodges, M.D., 950 East 59th St., Chicago 37.

### Alabama

**ALABAMA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. A. Meadows, Jr., M.D., Medical Arts Bldg., Birmingham 5.

### Arizona

**ARIZONA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. Lee Foster, M.D., 507 Professional Bldg., Phoenix. Annual meeting with State Medical Association; interim meeting in December.

### Arkansas

**ARKANSAS RADIOLOGICAL SOCIETY.** *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

### California

**CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY.** *Secretary*, H. R. Morris, M.D., 1027 D St., San Bernardino.

**EAST BAY ROENTGEN SOCIETY.** *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

**LOS ANGELES RADIOLOGICAL SOCIETY.** *Secretary*, George Jacobson, M.D., 1200 North State St., Los Angeles 33. Meets monthly, second Wednesday, Los Angeles County Medical Association Bldg.

**NORTHERN CALIFORNIA RADIOLOGICAL CLUB.** *Secretary*, H. B. Stewart, Jr., M.D., 2920 Capitol Ave., Sacramento. Meets last Monday of each month, September to May.

**PACIFIC ROENTGEN SOCIETY.** *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually at time of California State Medical Association convention.

**RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA.** *Secretary-Treasurer*, Donald R. Laing, M.D., 65 North Madison Ave., Pasadena 1.

**SAN DIEGO RADIOLOGICAL SOCIETY.** *Secretary*, C. W. Bruner, M.D., 2456 Fourth Ave., San Diego 1. Meets first Wednesday of each month.

**SAN FRANCISCO RADIOLOGICAL SOCIETY.** *Secretary*, I. J. Miller, M.D., 2680 Ocean Ave., San Francisco 27. Meets quarterly, at the University Club.

**SOUTH BAY RADIOLOGICAL SOCIETY.** *Secretary*, William H. Graham, M.D., 634 E. Santa Clara St., San Jose 12. Meets monthly, second Wednesday.

**X-RAY STUDY CLUB OF SAN FRANCISCO.** *Secretary*, Wm. W. Saunders, M.D., VA Hospital, San Francisco 21. Meets third Thursday at 7:45, Lane Hall, Stanford University Hospital.

### Colorado

**COLORADO RADIOLOGICAL SOCIETY.** *Secretary*, Parker Allen, M.D., Children's Hospital, Denver. Meets monthly, third Friday, at University of Colorado Medical Center or Denver Athletic Club.

### Connecticut

**CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary-Treasurer*, William A. Goodrich, M.D., 85 Jefferson St., Hartford 14. Meets bimonthly, second Wednesday.

**CONNECTICUT VALLEY RADIOLOGICAL SOCIETY.** *Secretary*, B. Bruce Alicandri, M.D., 20 Maple St., Springfield, Mass. Meets second Friday of October and April.

### District of Columbia

**RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY.** *Secretary*, Alvin C. Wyman, M.D., 5445 28th St., N.W., Washington. Meets third Wednesday, January, March, May, and October, at 8:00 P.M., in Medical Society Library.

### Florida

**FLORIDA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Hugh G. Reaves, M.D., Medical Arts Bldg., Sarasota. Meets in April and in October.

**GREATER MIAMI RADIOLOGICAL SOCIETY.** *Secretary*, E. Hampton Bryson, M.D., 273 Alhambra Circle, Coral Gables. Meets monthly, third Wednesday, 8:00 P.M., Veterans Administration Bldg., Miami.

### Georgia

**ATLANTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Albert A. Rayle, Jr., M.D., 490 Peachtree St. Meets second Friday, September to May.

**GEORGIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Robert M. Tankesley, M.D., 218 Doctors Bldg., Atlanta. Meets in November and at the annual meeting of the State Medical Association.

**RICHMOND COUNTY RADIOLOGICAL SOCIETY.** *Secretary*, Wm. F. Hamilton Jr., M.D., University Hospital, Augusta.

**Hawaii**

RADIOLOGICAL SOCIETY OF HAWAII. *Secretary*, Philip S. Arthur, M.D., Suite 42, Young Hotel Bldg., Honolulu. Meets third Friday of each month.

**Illinois**

CHICAGO ROENTGEN SOCIETY. *Secretary*, Elbert K. Lewis, M.D., 6337 S. Harvard Ave., Chicago 21. Meets at the University Club, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Stephen L. Casper, M.D., Physicians and Surgeons Clinic, Quincy.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, George E. Irwin, Jr., M.D., 427 N. Main St., Bloomington.

**Indiana**

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, John A. Ro'b, M.D., 23 East Ohio St., Indianapolis. Annual meeting in May.

**Iowa**

IOWA RADIOLOGICAL SOCIETY. *Secretary*, James T. McMillan, M.D., 1104 Bankers Trust Bldg., Des Moines. Meets during annual session of State Medical Society, and holds a scientific session in the Fall.

**Kansas**

KANSAS RADIOLOGICAL SOCIETY. *Secretary*, Willis L. Beller, M.D., 700 Kansas Ave., Topeka. Meets in the Spring with the State Medical Society and in the Winter on call.

**Kentucky**

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary*, Everett L. Pirkey, M.D., Louisville General Hospital. Meets monthly, second Friday, at Seelbach Hotel, Louisville.

**Louisiana**

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets second Tuesday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA. *Secretary-Treasurer*, J. T. Briere, M.D., 700 Audubon Bldg., New Orleans.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, W. R. Harwell, M.D., 608 Travis St. Meets monthly September to May, third Wednesday.

**Maine**

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Jack Spencer M.D., Maine General Hospital, Portland 4. Meets three times a year—Spring, Summer, and Fall.

**Maryland**

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary-Treasurer*, H. Leonard Warres, M.D., 2337 Eutaw Place, Baltimore 17. Meets third Tuesday, September to May.

MARYLAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, H. Leonard Warres, M.D., 2337 Eutaw Place, Baltimore 17.

**Michigan**

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary*, E. F. Lang, M.D., Harper Hospital, Detroit 1. Meets first Thursday, October to May, at Wayne County Medical Society club rooms.

**Minnesota**

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, John R. Hodgson, M.D., The Mayo Clinic, Rochester. Meets in Spring and Fall.

**Mississippi**

MISSISSIPPI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John W. Evans, M.D., 117 N. President St., Jackson, Miss. Meets monthly, third Tuesday, at 6:30 P.M., at the Rotisserie Restaurant, Jackson.

**Missouri**

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, James E. McConchie, M.D., First National Bank Bldg., Independence, Mo. Meets last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Francis O. Trotter, Jr., M.D., 634 North Grand Blvd. Meets on fourth Wednesday, October to May.

**Montana**

MONTANA RADIOLOGICAL SOCIETY. *Secretary*, Grant P. Raitt, M.D., 413 Medical Arts Bldg., Billings. Meets annually.

**Nebraska**

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James F. Kelly, Jr., M.D., 816 Medical Arts Bldg., Omaha. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

**New England**

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, Stanley M. Wyman, M.D., Massachusetts General Hospital, Boston 14. Meets monthly on third Friday, at the Harvard Club, Boston.

**New Hampshire**

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary*, Albert C. Johnston, M.D., 127 Washington St., Keene.

**New Jersey**

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Salomon Silvera, M.D., 921 Bergen Ave., Jersey City. Meets at Atlantic City at time of State Medical Society and midwinter in Elizabeth.

**New York**

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 2. Meets in January, May, and October.



**KINGS COUNTY RADIOLOGICAL SOCIETY.** *Secretary,* Solomon Maranov, M.D., 1450 51st St., Brooklyn 19. Meets fourth Thursday, October to April (except December), at 9:00 P.M., Kings County Medical Bldg.

**NASSAU RADIOLOGICAL SOCIETY.** *Secretary,* Frank Huber, M.D., 131 Fulton Ave., Hempstead, N. Y. Meets second Tuesday, February, April, June, October, and December.

**NEW YORK ROENTGEN SOCIETY.** *Secretary,* Jacob R. Freid, M.D., 1049 Park Ave., New York.

**NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Donald H. Baxter, M.D., Albany Hospital, Albany. Meets in the capital area second Wednesday, October, November, March, and April. Annual meeting in May or June.

**RADIOLOGICAL SOCIETY OF NEW YORK STATE.** *Secretary-Treasurer,* Mario C. Gian, M.D., 610 Niagara St., Buffalo. Meets annually with the State Medical Society.

**ROCHESTER ROENTGEN-RAY SOCIETY.** *Secretary-Treasurer,* A. Gordon Ide, M.D., 277 Alexander St. Meets at Strong Memorial Hospital, 8:15 P.M., last Monday of each month, September through May.

**WESTCHESTER RADIOLOGICAL SOCIETY.** *Secretary,* Charles G. Huntington, M.D., 170 Maple Ave., White Plains, N. Y. Meets third Tuesday of January and October and at other times as announced.

#### North Carolina

**RADIOLOGICAL SOCIETY OF NORTH CAROLINA.** *Secretary,* Waldemar C. A. Sternbergh, M.D., 1400 Scott Ave., Charlotte 2. Meets in April and October.

#### North Dakota

**NORTH DAKOTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* H. Milton Berg, M.D., Quain & Ramstad Clinic, Bismarck. Meets in the Spring with State Medical Association; in Fall or Winter on call.

#### Ohio

**OHIO STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* M. M. Thompson, Jr., M.D., 316 Michigan St., Toledo. Meets with State Medical Association.

**CENTRAL OHIO RADIOLOGICAL SOCIETY.** *Secretary,* Frank A. Riebel, M.D., 15 W. Goodale St., Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Columbus Athletic Club, Columbus.

**CLEVELAND RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Mortimer Lubert, M.D., Heights Medical Center Bldg., Cleveland Heights 6. Meets at 6:45 P.M. on fourth Monday, October to April, inclusive.

**GREATER CINCINNATI RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Chapin Hawley, M.D., 927 Carew Tower, Cincinnati 2. Meets first Monday of each month, September to June, at Cincinnati General Hospital.

**MIAMI VALLEY RADIOLOGICAL SOCIETY.** *Secretary,* W. S. Koller, M.D., 60 Wyoming St., Dayton. Meets monthly, second Friday

#### Oklahoma

**OKLAHOMA STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* John R. Danstrom, M.D., Medical Arts Bldg., Oklahoma City.

#### Oregon

**OREGON RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* John Wayne Loomis, M.D., 919 Taylor Street Bldg., Portland 5. Meets monthly, second Wednesday, October to June, at 8:00 P.M., University Club, Portland.

#### Pacific Northwest

**PACIFIC NORTHWEST RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4. Meets annually in May.

#### Pennsylvania

**PENNSYLVANIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

**PHILADELPHIA ROENTGEN RAY SOCIETY.** *Secretary,* Herbert M. Stauffer, M.D., Temple University Hospital, Philadelphia 40. Meets first Thursday of each month at 5:00 P.M., from October to May, in Thompson Hall, College of Physicians.

**PITTSBURGH ROENTGEN SOCIETY.** *Secretary-Treasurer,* Donald H. Rice, M.D., 4800 Friendship Ave., Pittsburgh 24. Meets monthly, second Wednesday, at 6:30 P.M., October to May, at Webster Hall.

#### Rocky Mountain States

**ROCKY MOUNTAIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* John H. Freed, M.D., 4200 East Ninth Ave., Denver 7, Colo.

#### South Carolina

**SOUTH CAROLINA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* William A. Klauber, M.D., Self Memorial Hospital, Greenwood. Meets with State Medical Association in May.

#### South Dakota

**RADIOLOGICAL SOCIETY OF SOUTH DAKOTA.** *Secretary-Treasurer,* Donald J. Peik, M.D., 303 S. Minnesota Ave., Sioux Falls. Meets during annual meeting of State Medical Society.

#### Tennessee

**MEMPHIS ROENTGEN CLUB.** *Secretary,* Harvey Thompson, M.D., 899 Madison Ave. Meets first Monday of each month at John Gaston Hospital.

**TENNESSEE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* George K. Henshall, M.D., 311 Medical Arts Bldg., Chattanooga 3. Meets annually with State Medical Society in April.

#### Texas

**DALLAS-FORT WORTH ROENTGEN STUDY CLUB.** *Secretary,* Otto H. Grunow M.D., 650 Fifth Ave., Fort Worth. Meets monthly, third Monday, 6:30 P.M., at the Greater Fort Worth International Airport.

**HOUSTON RADIOLOGICAL SOCIETY.** *Secretary,* Harry Fishbein, M.D., 324 Medical Arts Bldg., Houston 2.

**SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY.** *Secretary*, Hugo F. Elmendorf, Jr., M.D., 730 Medical Arts Building, San Antonio 5, Texas. Meets at Brook Army Medical Center, the first Monday of each month.

**TEXAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth. Next meeting Jan. 29-30, 1954, Dallas.

#### Utah

**UTAH STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City 1. Meets third Wednesday, January, March, May, September, November.

#### Virginia

**VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary*, P. B. Parsons, M.D., 1308 Manteo St., Norfolk 7.

#### Washington

**WASHINGTON STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Eva L. Gilbertson, M.D., 1317 Marion St., Seattle 4. Meets fourth Monday, September through May, at 610 Pine St., Seattle.

#### West Virginia

**WEST VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary*, W. Paul Elkin, 515-519, Medical Arts Bldg., Charleston. Meets concurrently with annual meeting of State Medical Society, and at other times as arranged by Program Committee.

#### Wisconsin

**MILWAUKEE ROENTGEN RAY SOCIETY.** *Secretary-Treasurer*, Jerome L. Marks, M.D., 161 W. Wisconsin Ave., Milwaukee 1. Meets monthly on fourth Monday at the University Club.

**SECTION ON RADIOLOGY, STATE MEDICAL SOCIETY OF WISCONSIN.** *Secretary*, Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee 2. Meets in October with State Medical Society.

**UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE.** Meets first and third Thursday at 4 P.M., September to May, Service Memorial Institute.

**WISCONSIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, W. W. Moir, M.D., Sheboygan Memorial Hospital, Sheboygan.

#### Puerto Rico

**ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA.** *Secretary*, Rafael A. Blanes, M.D., Box 9724 Santurce, Puerto Rico.

#### CANADA

**CANADIAN ASSOCIATION OF RADIOLOGISTS.** *Honorary Secretary-Treasurer*, D. L. McRae, M.D. *Asso-Hon. Secretary-Treasurer*, Guillaume Gill, M.D. *Central Office*, 1555 Summerhill Ave., Montreal 25, Quebec. Meets in January and June.

**LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES.** *General Secretary*, Origène Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday of each month.

#### CUBA

**SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA.** *Secretary*, Dr. Rafael Gómez Zaldívar. Offices in Hospital Mercedes, Havana. Meets monthly.

#### MEXICO

**SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA.** *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, Mexico, D.F. Meets first Monday of each month.

#### PANAMA

**SOCIEDAD RADIOLOGICA PANAMEÑA.** *Secretary-Editor*, Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.



## ABSTRACTS OF CURRENT LITERATURE

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## ROENTGEN DIAGNOSIS

### THE HEAD AND NECK

**Laminagraphy in the Study of Cerebral Sulci and Cisternal Spaces.** Fermo Mascherpa and Guido Lombardi. *Radiol. med. (Milan)* 38: 1160-1166, December 1952. (In Italian)

The authors have employed laminagraphy for the study of the sulci and cisternal spaces after encephalography. This technic was used because it eliminates confusing superimposition of shadows.

Normal laminagrams taken at various levels in the anteroposterior projection and laminagrams of two pathological cases are presented. The symmetry of the sulci and cisternal spaces under normal conditions is in remarkable contrast to the distorted appearance in the presence of small space-occupying lesions. The radiographic reproductions are excellent and suggest that this may be one of the most fruitful applications of laminagraphy.

Nine roentgenograms; 7 drawings.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Agenesis of the Corpus Callosum Diagnosed During Life. Review of the Literature and Presentation of Two Cases.** Malcolm B. Carpenter and William H. Druckemiller. *Arch. Neurol. & Psychiat.* 69: 305-322, March 1953.

A review of the literature disclosed 43 cases in which the diagnosis of agenesis of the corpus callosum was made by encephalography during life. The authors report 2 additional cases which came under their observation.

The diagnosis of agenesis of the corpus callosum apparently has been made only by encephalographic studies. The roentgenographic findings in order of frequency are dorsal extension and dilatation of the third ventricle, wide separation of the lateral ventricles, dilatation of the posterior horns of the lateral ventricles, and angular dorsal margins and concave mesial borders of the lateral ventricles.

Review of the reports in the literature, as well as the authors' own cases, showed the physical and neurological findings to vary widely. Thus, this material does not support the theory of a specific syndrome of the corpus callosum. Grand mal epilepsy was the initial symptom in 42 per cent of the cases and occurred sometime during the course of illness in 60 per cent. The initial symptoms appeared before two years of age in 53 per cent of the cases, and in only 2 cases (those being currently reported) were symptoms first evident after the age of twenty.

Five roentgenograms; 2 tables.

DEAN W. GEHEBER, M.D.  
Baton Rouge, La.

**Tumors of the Posterior Portion of the Third Ventricle.** Robert W. Rand and Lloyd J. Lemmen. *J. Neurosurg.* 10: 1-18, January 1953.

A study of 32 patients having neoplasms of the posterior portion of the third ventricle, seen at the University of Michigan Hospital from 1930 to 1951, forms the basis of this report. It includes tumors originating from the posterior wall of the third ventricle and the pineal body, but not those of the thalamus, splenium of

the corpus callosum, choroid plexus, or anterior portion of the third ventricle.

Probably the most common presenting symptoms were those of increased intracranial pressure—headache, nausea, vomiting, papilledema, and blurring of vision. Secondly, signs of regional anatomical involvement proved helpful in localizing the lesion. Frequently, such signs were limitation of upward gaze and variation in pupillary responses. The anatomical basis for these and other clinical features is discussed.

The size of the tumor may be suggested by certain clinical findings. Loss of downward conjugate deviation of the eyes, impairment of hearing, and cerebellar signs indicate posterior extension of the growth. Inferior extension may be manifested by hypersomnia or precocious puberty.

Valuable diagnostic aid is furnished by plain roentgenograms when there is calcification in the pineal gland or its vicinity. Ventriculography affords the most accurate information regarding localization and size of tumors in this area. There was no apparent correlation, however, between the roentgenographic findings and histologic structure. Angiography was not used in any of the series.

Nineteen of the authors' cases were verified histologically: 9 pinealomas (one proved ectopic), 5 pinealoblastomas, 4 teratomas, and 1 undifferentiated glioma. The remaining 13 were diagnosed on the basis of the clinical and ventriculographic findings.

Those patients in whom surgical removal of the tumor was attempted died usually a short time after surgery. A more conservative approach consists of ventriculostomy or ventriculocisternostomy in combination with x-ray therapy. The latter course is recommended for a maximal survival period with minimal neurologic deficit.

Fourteen illustrations, including 3 roentgenograms; 2 tables.

ALLIE WOOLFOLK, M.D.  
Pittsburgh, Penna.

**Meningiomas of the Anterior Clinoid Process as a Cause of Unilateral Loss of Vision. Surgical Considerations.** Alfred Uihlein and Robert D. Weyand. *Arch. Ophth.* 49: 261-270, March 1953.

Meningiomas of the anterior clinoid process grow slowly and are relatively silent. If not recognized early, these tumors attain such a size before coming to the surgeon's attention that total removal is attended with much risk. To prevent recurrence, total removal of the tumor is necessary. The authors believe that early neurosurgical consultation, the making of stereolateral roentgenograms of the skull, and accurate performance of tests of the visual fields are indicated in every case in which a patient complains of unilateral visual impairment. If this plan is followed, an early diagnosis can be made and the tumors can be removed rather easily, with few complications and a comparatively low mortality rate, before irreparable loss of vision occurs.

During the twenty-one-year period from 1930 to 1950, 52 patients who had meningiomas arising from the region of the anterior clinoid process were treated surgically at the Mayo Clinic. The average duration of symptoms before the diagnosis was made was four years. A history of loss of vision was obtained in 48

cases. In 30 cases this began as a unilateral defect and progressed to complete loss of useful vision in the eye concerned. In 15 of the 30 cases loss of vision also occurred in the opposite eye, usually causing the patient again to seek medical attention. Other symptoms were puffiness of one eyelid, anosmia, mental change, photophobia, diplopia, episodes of giddiness, and weakness of the legs.

The results of routine x-ray examination of the skull suggested the presence of a tumor of the brain in 36 patients. Erosion of the sella turcica or the parasellar region was noted in 22 cases. In 14 instances the roentgen findings indicated the presence of an osteoma involving the anterior clinoid process and the surrounding structures. In 1 case in which an osteoma was found at operation, roentgenograms showed marked thickening of the sphenoid bone, which was regarded as an anatomic variant. In 3 cases a calcified tumor was observed roentgenographically. Ventriculographic studies were made in 3 cases, and a pneumoencephalographic examination was made in 1. In all 4 instances evidence of a space-occupying lesion was demonstrable. Angiography was carried out in 3 cases; in 2 of these the angiograms disclosed posterior displacement and straightening out of the carotid siphon, findings which were considered diagnostic of a tumor. In the remaining case the angiogram was technically unsatisfactory.

Among the 52 cases there were 17 postoperative deaths in the hospital, a mortality rate of 32.7 per cent. Of the 32 patients whose condition it was possible to follow, 5 died between one and seven years after operation, probably of recurrence. Seventeen were well at the time of the report, and, although they had unilateral anosmia and decreased vision in one eye, they were able to read and work. Nine of the 17 had been well for more than six years. The remaining 10 patients were unable to work because of mental impairment, hemiparesis, or blindness.

Three roentgenograms; 1 photomicrograph; 1 drawing; 2 tables.

**Diagnosis of Tumors of the Pituitary Body.** John Raaf and Winchell McK. Craig. *West. J. Surg.* 61: 93-101, March 1953.

Neoplasms in and near the pituitary body vary greatly in their amenability to treatment. For chromophobe adenomas, intracranial operations are relatively safe, but the risk increases with extrasellar extension of the tumor. For this reason early diagnosis is highly desirable.

Chromophobe adenomas constitute approximately 70 to 80 per cent of the pituitary adenomas. These tumors commonly give rise to a clinical picture described as hypopituitarism or "pituitary eunuchism," with diminution of libido and impotence in the male and amenorrhea in the female. Expansion of the adenoma leads to rupture of the dural capsule and pressure on the optic chiasm, with consequent visual disturbances.

The roentgenographic findings are usually limited to enlargement of the sella turcica, which has been described as "ballooning." This was observed in 117 of 124 cases seen at the Mayo Clinic, from which this report comes. As the intrasellar mass enlarges, the posterior clinoid processes become thinner, and occasionally the anterior clinoids appear to be elevated. Increased intracranial pressure of long standing from other causes may also produce destruction of the sella, but a generalized increase in pressure results in a

flattening and elongation of the structure rather than ballooning. In the chromophobe adenoma, calcification occasionally occurs in the sella or the suprasellar region.

To be differentiated from chromophobe adenoma are craniopharyngioma, meningioma, arachnoiditis, parasellar aneurysms, and primary gliomas.

Acidophile or eosinophile adenomas are less common than the chromophobe variety. Excessive production of the growth hormone results in gigantism or acromegaly. These changes usually occur long before the adenoma has reached a size sufficiently great to exert pressure on neighboring structures, and sellar enlargement and changes in visual fields are therefore less common than in the chromophobe adenomas.

The condition known as "pituitary basophilism" or Cushing's disease has been productive of much discussion during the past two decades, some holding, with Cushing, that the entire syndrome is attributable to a basophile adenoma and others that it is of adrenocortical origin.

Adenocarcinoma of the pituitary is rare. In Cushing's series it constituted 3 per cent of all pituitary neoplasms. The tumors have a tendency to invade surrounding structures but do not often metastasize. Clinically, the patients fall into two groups: in one the findings are identical with those of a chromophobe adenoma; in the other, the outstanding manifestations are trigeminal involvement and ocular palsy.

Five roentgenograms; 4 tables.

L. R. JAMES, M.D.  
Boston, Mass.

**Cerebral Calcification Epilepsy. Report of a Case of Epilepsy Caused by a Calcified Hamartoma of the Brain.** W. Stewart Alexander. *J. Neurosurg.* 10: 69-74, January 1953.

The case of a 40-year-old mentally retarded white male who had been subject to intermittent epileptic seizures since the age of five years is reported. Roentgenograms of the skull demonstrated an ovoid calcified area in the right temporal lobe and a smaller similar area in the left parietal region. In the anteroposterior view, these were shown to be crescent-shaped and to lie near the surface of the lobe. A right craniotomy was performed and the temporal calcification was removed, with a block of the surrounding tissue. The patient improved symptomatically, although he had two episodes of seizures within a two-and-a-half-year period following the operation.

The relationship of the calcifications to a mass of blood vessels, as demonstrated microscopically, suggests a similarity to the condition observed by Geyelin and Penfield (*Arch. Neurol. & Psychiat.* 21: 1020, 1929) in a father and his four children, designated "endarteritis calcificans cerebri." The pathological appearance was similar and there was a familial factor. These cases differ in the latter respects, and in the multiplicity of the lesions, from racemose angiomas and angiomas of the Sturge-Weber type, as well as from Penfield and Ward's "hemangioma calcificans."

The author believes that in his patient the condition developed as a degenerative change in an existing vascular abnormality. The alternative name of "calcified subcortical hamartoma" is suggested.

Three roentgenograms; 1 photograph; 2 photomicrographs.

PAUL R. NOBLE, M.D.  
Pittsburgh, Penna.

**The Aneurysmal Origin of Nonfatal Subarachnoid Hemorrhage. An Angiographic Survey of 53 Cases.** Wallace B. Hamby. *J. Neurosurg.* 10: 35-37, January 1953.

In 1947, the author reported a series of 130 cases of spontaneous subarachnoid hemorrhage from the records of Buffalo General Hospital seen between the years 1929 and 1945 (*J.A.M.A.* 136: 522, 1948. Abst. in *Radiology* 53: 125, 1949). The cause of bleeding was determined at autopsy or operation in 47 cases; in 44 (or 93.6 per cent) it originated from intracranial aneurysms. It seemed "reasonable to assume that in the unproved cases, the percentage due to aneurysms would parallel that of proved cases." Opinions of others varied in regard to this assumption.

Since the earlier report, cerebral angiography has been employed with increasing frequency in cases of hemorrhages not immediately fatal. Among 53 cases, angiograms revealed aneurysms in 22 (41 per cent) and an arteriovenous malformation in 1 case. In 4 cases, angiograms failed to indicate aneurysms found later at autopsy. One of these was on the posterior communicating artery; the other 3 were on the anterior communicating complex.

Despite certain shortcomings and "imperfect utilization" in this series, the author considers angiography the best adjuvant now available for diagnosis of lesions causing spontaneous subarachnoid hemorrhage. Visualization of the entire intracranial tree is necessary to demonstrate the greatest possible number of aneurysms. Even then, all may not be visualized, due to the dynamics involved, size of the lesions, and possible thrombosis in some of the aneurysms.

ALLIE WOOLFOLK, M.D.  
Pittsburgh, Penna.

**Temporary Hemiplegia from Cerebral Injection of Diodrast During Catheter Aortography. Report of Two Cases.** E. Converse Peirce, 2nd. *Circulation* 7: 385-392, March 1953.

Temporary hemiplegia occurred in 2 cases in which 70 per cent Diodrast was injected directly into the aortic arch through a catheter placed in the arch by way of the femoral artery. In 1 case the catheter was shown to have entered the innominate artery. In both instances the Valsalva maneuver was carried out during the procedure to deliberately slow the circulation and hence lessen the dilution of the medium.

Because of the temporary nature of the hemiplegia (hours) and the lack of a clear-cut response to hypertonic glucose and stellate ganglion block, the author believes the damage was the result of interference with the blood-brain barrier from direct action of the concentrated Diodrast.

A number of recommendations are offered for prevention of this complication of aortography: (1) Do not inject the medium in such a way that the maximum concentration is in the arch unless this is essential to the success of the procedure. (2) If a catheter is employed, ascertain where the tip is by a positioning film and do not have it in one of the aortic arch branches if 70 per cent Diodrast is to be used. (3) Do not use the Valsalva maneuver whenever Diodrast may enter the cerebral circulation. (4) Compress the carotids during the injection. (5) Use the smallest possible amount of contrast medium. (6) Use lower concentrations in children.

A good review of the literature on complications incident to Diodrast injection is included.

Six roentgenograms. ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**The Effect of Contrast Media on the Blood-Brain Barrier.** Robert C. Bassett, James S. Rogers, Glenn R. Cherry, and Carl Gruzhit. *J. Neurosurg.* 10: 38-47, January 1953.

It is well known that cerebral angiography is not without morbid and even fatal sequelae. The authors used the basic aniline-dye method employed by Broman and Olson (see *Acta radiol.* 30: 326, 1948; 31: 321, 1949. Abst. in *Radiology* 53: 624, 1949; 54: 767, 1950) to study the breakdown of the blood-brain barrier (BBB), but modified the method by having the dye in circulation before rather than following the injection of the contrast medium. The subjects used were 162 dogs and 12 rabbits.

The experiments showed the basic lesion resulting from injection of 35 per cent Diodrast to be a disturbance of cerebral vascular permeability. The concentration of the drug and duration of exposure to it are of primary importance in determining the extent of this lesion. Twenty-five per cent sodium iodide, 70 per cent Urokon, and 70 per cent Diodrast all produced massive breakdown of the BBB. The sodium iodide and Urokon, when given in very large doses (50 c.c.), also produced a marked hemorrhagic effect. Breakdown of the BBB is accompanied by passage of protein-rich fluid into the extravascular compartment of the brain, and by a rise in cerebrospinal fluid pressure. It is postulated that in patients with intrinsic vascular diseases, subsequent spasm, thrombosis, and thromboembolism are probably secondary to the initial alteration of permeability.

The authors suggest that greater care be exercised in selection of patients for angiography and that minimally effective concentrations of contrast media be used over the shortest possible period of time.

Four illustrations, including 1 roentgenogram; 5 tables. C. R. PERRYMAN, M.D.  
Pittsburgh, Penna.

**Malignant Tumors of the Nasal Fossa and Ethmoid. A Radiologic Study. An Attempt at Topographic Classification.** P. Eggimann. *Radiol. clin.* 22: 65-96, March 1953. (In French)

This report is based on the study of 154 patients with malignant tumors of the nasal fossa and of the ethmoid. Of 122 tumors examined histologically, 41 were squamous-cell epitheliomas, 34 cylindrical-cell epitheliomas, 9 cylindromas, 6 malignant melanomas, 20 lymphosarcomas and reticulosarcomas, 5 sarcomas of other types, 2 neuroblastomas, and 5 tumors of undetermined origin.

For radiologic study, postero-anterior, lateral, and submento-vertical views are helpful, and tomography may be of great value. Radiologic signs include opacity, osseous destruction, and expansion or displacement of bony boundaries. Opacification of one or both maxillary sinuses may occur.

There is great diversity of histologic classification of these tumors. A topographic classification should be of value, but it must be admitted that it may be difficult to detect the origin of a given tumor. At times, during radiotherapy, a tumor may be seen receding toward its



point of origin. The topographic classification suggested here includes superior and inferior planes separated by the middle nasal choana. In the superior group are tumors of the anterior ethmoid or ethmoid-frontal area, tumors of the ethmoid proper, and posterior ethmoid or ethmoido-sphenoidal tumors. The most interesting tumors of the inferior group, from the radiological point of view, are those of the external wall.

At the Curie Foundation, roentgen therapy is used on inoperable cases and postoperatively in surgical cases. Factors are 180-200 kv., 1.0 mm. Cu filter, and 50 to 60 cm. distance. Three fields are treated, with 4,000 to 5,000 r skin dose to each field in nine to twelve weeks. This gives a tumor dose of about 5,000 r. Slightly lower dosage is used in lymphosarcoma, but a tumor dose of 4,000 r is advisable.

Of 33 patients with malignant epithelial tumors treated by radiotherapy alone, only 12 lived two years or more. Only limited epitheliomas and some cylindromas appear to have a good prognosis; localized lymphosarcomas may also be controlled. Five patients with lymphosarcoma have survived five years or longer, and in all of these the tumor was localized when treatment began. Very few patients with epitheliomas live five years, but relief of symptoms is definite.

Thirty-one roentgenograms; 3 drawings; 5 tables.

CHARLES M. NICE, M.D.  
University of Minnesota

**Preliminary Results of Orbital Phlebography.** P. Bétoulières, R. Paleirac, and Ch. Boudet. *J. de radiol. et d'électrol.* 34: 160-165, 1953. (In French)

For phlebography of the orbital veins, a small incision is made over the angular vein under local anesthesia and from 7 to 10 c.c. of 50 per cent Diodone is injected, following which lateral and anteroposterior roentgenograms (occipital projection at 25° angle) are obtained. The veins of the orbit, the cavernous sinus, pterygoid plexus, and subcutaneous cranial veins may thus be visualized.

The normal radiographic anatomy is described and illustrated, and a case is reported in which a carcinoma of the lacrimal gland produced displacement and obstruction of the superior orbital vein.

Seven roentgenograms; 9 drawings.

CHARLES M. NICE, M.D.  
University of Minnesota

**Carotid Cavernous Fistula with Signs on Contralateral Side. Case Report.** Miguel Ramos and Lester A. Mount. *J. Neurosurg.* 10: 178-182, March 1953.

A case is presented of a fistula of the right internal carotid artery into the right cavernous sinus, draining through the anterior part of the circular sinus to the left cavernous sinus and left superior ophthalmic vein. The clinical findings consisted of a congestion of the left eyelid, a left non-pulsating exophthalmos, and a bruit over the left eye. Apparently the patient's right ophthalmic vein did not join with the cavernous sinus.

The bruit over the left eye was not obliterated by bilateral carotid compression, because of a large right posterior communicating artery which carried blood to the fistula from the basilar artery. These changes were demonstrated by cerebral angiography.

Four arteriograms.

HOWARD L. STEINBACH, M.D.  
University of California

## THE CHEST

**Histoplasmosis with Particular Attention to Histoplasmosis of the Lungs.** A. Jakob and E. Krisch. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 287-290, March 1953. (In German)

Clinically, a distinction can be made between primary pulmonary histoplasmosis and a generalized form. The latter shows an acute, a subacute, and a chronic phase. Irregular fever, anemia, loss of weight, enlargement of the liver and spleen, ulcerative changes of the skin and mucous membranes, small intestines and colon, and, above all, a typical or atypical infiltration of the lungs are characteristic signs. Pathologically, the manifestations of the generalized form are to be found for the most part in the reticulo-endothelial system, where they produce granulomatous changes, mainly in the bone marrow, lungs, liver, spleen, and lymph nodes. The microscopic examination of a section of the spleen will show large reticulum cells in which the nucleus is forced to the periphery, while the rest of the protoplasm is filled with small round structures resembling specks of pepper.

The diagnosis is mainly established by the histoplasmin skin test and by serologic tests. The skin test particularly has made it possible to recognize many cases that were previously believed to be of tuberculous origin. A positive skin test, however, is not a measure of the activity of the process.

In the acute stage of the disease with pulmonary manifestations, it is extremely difficult to make a diagnosis from the roentgenologic appearance. The findings are usually those of a lobar pneumonia or of numerous individual bronchopneumonic foci. Within about four to thirty months after the beginning of the disease, calcifications occur in the individual foci, and then the suspicion of histoplasmosis will be aroused. The diagnosis is definitely made if the histoplasmin test is positive and the tuberculin test is negative.

In the differential diagnosis of histoplasmosis, other fungous infections, tuberculosis, Hodgkin's disease and Boeck's sarcoid must be considered. It may be important to remember that the calcifications of histoplasmosis develop mostly in the lower and in the middle sections of the lungs, seldom involving the apices, while in tuberculosis the changes are largely in the upper lobes.

Three roentgenograms; 1 photomicrograph.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**Histoplasmosis. Report of Two Cases.** Robert Charr. *Am. Rev. Tuberc.* 67: 376-384, March 1953.

The mouth and larynx are frequent sites of initial infection in histoplasmosis. Two cases are reported in which a diagnosis was made antemortem by means of biopsy of a local lesion. One lesion was in the larynx, while the other was on the soft palate. One patient gave a positive histoplasmin skin test and complement-fixation test; these tests were negative in the other patient and are not believed to be reliable in the diagnosis of the disease.

In one patient the chest roentgenogram showed superior mediastinal enlargement for several years, but frank pulmonary involvement was not noted until three months before death. The other patient had pulmonary tuberculosis with cavitation, which produced the only roentgenographic findings. There is no typical

roentgenographic appearance in pulmonary histoplasmosis. In some instances there is accentuation of markings extending out from the hili; in others, areas of pulmonic consolidation are observed. Widespread nodular lesions are fairly common, and some cases simulate cavitary tuberculosis. Pulmonary sarcoidosis is also simulated by histoplasmosis, with involvement of mediastinal nodes as well as the pulmonary parenchyma.

Three roentgenograms. JOHN H. JUHL, M.D.  
Minneapolis, Minn.

**A Histoplasmin and Tuberculin Study of Psychiatric Patients Having Abnormal Chest Roentgenograms.** Millard A. Troxell. *Minnesota Med.* 36: 235-239, March 1953.

The histoplasmin and tuberculin reactions of 103 psychiatric patients with abnormal chest roentgenographic findings were studied in a state hospital in Minnesota. Ninety-five patients were tuberculin-positive and 40 were histoplasmin-positive. Complement-fixation tests for histoplasmosis were done on all the patients skin-tested, and the results were entirely negative. Seven patients were both histoplasmin- and tuberculin-negative. Only one case was histoplasmin-positive and tuberculin-negative.

Considerable doubt has been raised regarding the usefulness of the histoplasmin test. Saslaw and Prior (*Ohio State M. J.* 48: 229, 1952) believe that a positive skin test may serve to include histoplasmosis in the differential diagnosis but state that there may be no skin reaction in fulminating or disseminated disease. As to the tuberculin test, it should not be considered negative until it has been carried to a 1:1,000 dilution of tuberculin.

While the histoplasmin skin test and the histoplasmosis complement-fixation test did not help establish the diagnosis in cases with "suspicious" roentgen findings, they did indicate a relatively high incidence of histoplasmin reactors in the institution where the study was conducted. Thirty-nine per cent of the patients tested were positive, as opposed to incidences of 4 to 10 per cent previously found in the immediate area.

One table. SEYMOUR A. KAUFMAN, M.D.  
Boston, Mass.

**Pseudosyphilitic (Wassermann-Positive) Virus Pneumonia. Experiences with 37 Cases from 1940 to 1952.** H. Herzog and W. Pulver. *Schweiz. med. Wchnschr.* 83: 227-234, March 7, 1953.

Pseudosyphilitic "hilifugal" pneumonia was first described in 1936 by Fanconi, who reported 4 cases in undernourished children (*Schweiz. med. Wchnschr.* 66: 821, 1936. *Abst. in Radiology* 28: 647, 1937). The authors recount their experience with 37 cases. The disease begins with fever lasting for seven to ten days, associated with bronchitis or pneumonia-like symptoms and physical findings. Radiologically demonstrable "lung infiltrates" appear either during or after this period and disappear after three to five weeks, whereas enlargement of one or both hili remains for another one or two weeks. Leukocytosis, usually between 10,000 and 15,000, with a shift to the left, and an elevation of the sedimentation rate up to 60 mm./hr. were noted. The predominant age group was twenty to thirty-five years (total range one to forty years). Twenty-seven patients were males; 10 were females.

These cases represent 3.7 per cent of all non-tuberculous pneumonias observed between 1940 and 1952 at the Luzerne Canton Hospital. Common to all cases was a positive Wassermann reaction; other serum tests for syphilis (including the Kahn test) were frequently though not invariably positive. The cerebrospinal fluid showed a positive reaction in only 3 cases (without neurological findings). The serum reaction became positive with the appearance of the lung infiltrate and outlasted it usually by three or four weeks, occasionally by several months. Spontaneous regression of the reaction thereafter is characteristic.

Treatment is symptomatic; antibiotics, when tried, were not clearly beneficial. There were no fatalities.

The radiographic findings, as illustrated, vary considerably and seem to resemble segmental pneumonitis or lobular pneumonia.

Eight roentgenograms; 1 table summarizing the findings in the 37 cases.

GERHART S. SCHWARZ, M.D.  
New York, N. Y.

**Pseudotumoral Pulmonary Syphilis.** J. Royer and A. Gloaguen. *J. franç. de méd. et chir. thorac.* 7: 268-271, 1953. (In French)

A 40-year old male had an ovoid shadow in the right lung resembling either a tumor or tuberculosis. Failure to find more definite evidence for either of these diagnoses, along with a positive serologic test for syphilis, led to the institution of antilutetic therapy. Within six weeks the chest roentgenogram was clear.

Three roentgenograms.

CHARLES M. NICE, M.D.  
University of Minnesota

**Prolonged Pulmonary Forms of Bornholm's Disease.** A. Breton. *J. franç. de méd. et chir. thorac.* 7: 263-268, 1953. (In French)

Bornholm's disease, or epidemic pleurodynia, is probably due to a virus, and is usually of short duration. Some cases run a more prolonged course, up to thirty months. In the first few days of the disease, segmental pulmonary shadows similar to those caused by viruses may be seen. Some patients have a series of remissions and exacerbations of varying duration over a period of two to two and one-half years. The fact that pleural reaction may occur in this disease may lead to suspicion of tuberculosis in some cases.

Two roentgenograms. CHARLES M. NICE, M.D.  
University of Minnesota

**Changes in the Bronchi in Silicosis and Silico-tuberculosis.** G. Worth and W. Heinz. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 263-272, March 1953. (In German)

The authors have investigated the small peripheral ramifications of the bronchial tree of the involved area in cases of silicosis and silicotuberculosis. The bronchographic demonstration of these fine bronchial branches in the presence of fibrosis has been made possible by the introduction of highly viscous, water-soluble contrast materials which are relatively harmless and quickly resorbed. Very helpful has been the development of an excellent local anesthetic of low toxicity for the mucous membrane, called Salicain.

The indications for bronchographic examination in the cases of silicosis seen by the authors were an un-

explained discrepancy between the clinical and the roentgen findings, bronchitis of undetermined origin, and changes in the blood picture indicating inflammatory processes not explained by other methods of examination. The procedure was used, also, in an attempt to differentiate silicotic processes from tumors and cystic degeneration of the lungs. In all cases, bronchographic examination is a last resort, to be used only after a routine x-ray examination, including laminagraphy. Contraindications to the use of bronchography are high fever, poor general condition, danger of hemorrhage, active tuberculosis, with cavitation, and gangrene of the lungs.

Fifty patients were examined: 42 had only silicosis; in 8, tuberculosis was also present. The changes found were classified as deformities of the bronchial wall, dilatation and narrowing of the bronchial lumen, bronchial occlusion, atelectasis, kinking and distortion of the bronchial tree, and the formation of cavities. The most common findings were those of a deforming bronchitis, with an irregularly serrated contour of the bronchial wall, more or less marked variations in the caliber, bronchospasm, and bronchoparalysis. Sometimes, dilated segments alternated with areas of constriction, producing the appearance of a "rosary." In 44 cases, changes typical of such a deforming bronchitis could be demonstrated but in only 20 of these could bronchitis be diagnosed clinically. Twenty-four cases showed normal clinical findings on auscultation.

Bronchiectases were found as the end-result of a chronic deforming bronchitis or as a consequence of the mechanical action of cirrhotic shrinking fibrotic masses, or in association with stenoses and occlusions with retention of bronchial secretions producing damage to the bronchial wall and subsequent increase in caliber, due to the elastic retraction of the pulmonary tissue.

Stenosis and occlusion of a bronchus may occur as the result of a chronic deforming bronchitis or through compression by fibrotic silicotic nodes outside of the bronchus. Kinking and distortion of a bronchus were frequently observed.

Localized emphysema could be demonstrated by delay in filling and a diminution of the movement of the contrast material in various phases of respiration. The poor alveolar filling gave the terminal ramifications of the bronchial branches an uneven, changing, irregular appearance. Cavitation was better demonstrated by laminagraphic examination. Bronchial spasm was only rarely seen.

The resorption of the contrast material gives some information regarding the function of the mucous membrane of the bronchial tree. Ordinarily, twenty to forty-five minutes after bronchography, the opaque material is no longer demonstrable. In cases of silicosis with bronchiectasis, atelectasis, and cavitation, there was often a delay in resorption of the medium.

In conclusion, it may be said that bronchographic examination with a water-soluble contrast medium gives valuable information about the morphological changes of the bronchial tree, such as stenoses, dilatation, bronchiectasis, occlusion, distortion, etc., which cannot easily be obtained by other means.

This article is well written and clearly illustrated. It should be read in the original text by anybody who is interested in this phase of silicosis.

Nine roentgenograms.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**The Lung Structure in Roentgenograms of Rare Pneumoconioses.** R. Haubrich and B. Schuler. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 272-281, March 1953. (In German)

Pneumoconiosis in its late stages can usually be differentiated from other lung conditions, and in many cases the specific damaging agent can be identified from the chest film. In the early stages, it may be impossible to make the diagnosis at all.

The authors present several cases of the rarer pneumoconioses and demonstrate some of the roentgenologic characteristics which help to make an early differential diagnosis possible.

**Corundum Lung:** Eight cases of corundum lung were observed. In all, the initial findings included streaky bronchial thickening, with a widening of the hilar shadow on each side. Subsequently, fine nodules in the alveoli were added, and in the late stages various large bronchopneumonic infiltrations were found scattered over the lungs, or a bullous emphysema developed. Clinically, these cases present a picture of severe chronic asthmatic bronchitis. All patients complained of shortness of breath. The changes are similar to those found in aluminum pneumoconiosis. As a matter of fact, even a simple chronic bronchitis with bronchiectasis may closely resemble the early stages of this type of disease.

**Soot Lung:** The authors observed 6 cases of soot lung. The roentgenograms show a characteristic net-like, honeycomb appearance of the lung structure, with slight thickening but no induration. Interspersed are extremely small nodules. One patient had a history of eighteen years of exposure, with only slight roentgenographic changes. Although the roentgen findings may not be very obvious, large perivascular and peribronchial soot deposits may be found on pathologic examination. The differential diagnosis is difficult. The changes are not striking even after long exposure, and other diseases of the lung with a similar anatomical distribution may produce the same appearance, as, for instance, Boeck's sarcoid. A similar picture may also be present in Hodgkin's disease of the lung and neoplastic lymphangitis.

**Iron Ore Lung and Ochre Dust Lung:** These conditions are characterized by fine dust deposits all over the lungs, closely resembling hemosiderosis or true siderosis. In the late stages, however, the pneumoconiosis of the iron ore group will be characterized by scar formation and indurations in the periphery of the upper and middle lobe, while the hemosiderotic congestive lung is recognized by perihilar thickening. In the early stages, a differential diagnosis may be impossible. Boeck's sarcoid in a miliary form without much fibrosis may produce a similar appearance. The anatomical change in the iron ore lung consists in an alveolar desquamation with only slight interstitial connective-tissue reaction. In Boeck's sarcoid, there is a nodule-like miliary lupoid which cannot be differentiated roentgenologically from true pneumoconiosis.

Sixteen roentgenograms.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**The Pulmonary Tuberculoma.** K.-H. Willmann. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 281-287, March 1953. (In German)

Circular tuberculous foci and solitary pulmonary

lesions may produce great differential diagnostic difficulties. They may remain stationary for years, suddenly becoming reactivated and increasing in size. The adjoining lung structure usually shows little reaction. The lesions occur mostly in the third decade of life and are predominantly localized in the right lung.

There are three possibilities of development. A large primary focus may fail to resorb completely and a connective-tissue capsule may develop around it. A post-primary caseous pneumonia may become localized and demarcated by a connective-tissue membrane. A cavity may close as a result of occlusion of the draining bronchus, becoming filled with caseous material which may be partially calcified.

The author describes 5 cases of tuberculoma that were operated upon, representing 5 per cent of all surgical operations for tuberculosis.

The clinical findings are relatively meager. The diagnosis is made by x-ray examination. The lesion is more or less round or oval, measuring from 2 to 8 cm. in diameter, and is usually sharply defined. If other evidences of tuberculosis are found in the lungs, the diagnosis of a tuberculoma becomes more probable, but the simultaneous appearance of tuberculosis and a malignant process must be kept in mind. Calcific deposits within the tuberculoma are important. They point strongly to a diagnosis of tuberculoma, since malignant lesions seldom show calcification. Calcification may occur in the form of homogeneously distributed deposits, giving the appearance of a mulberry, or it may produce a shell-like outer capsule. Areas of liquefaction or even formation of small cavities give the lesion an uneven character. In contradistinction to true cavitation, the cavity of a tuberculoma appears to be uneven, irregular, and often marginal.

The differential diagnosis between a tuberculoma and a tumor is often impossible. Among the benign lesions, fibromata, lipomata, congenital or acquired cysts, echinococcus cysts, hemangiomas, and gummata have to be considered. Inflammatory processes, as pneumonia, abscess, and encapsulated pleuritic empyema, etc., must be ruled out. Most important is the differential diagnosis between a tuberculoma and a malignant lesion. Solitary pulmonary metastases of tumors of the prostate gland, the testes, the kidneys, and the adrenals may produce similar circular lesions. If these are multiple, the diagnosis of tumor metastases becomes much more probable. A primary sarcoma of the lungs may have a similar appearance, producing a round shadow which only gradually increases in size. A localized carcinoma near the hilus soon leads to atelectasis, which is rare in tuberculoma, but carcinoma developing near the periphery of the lungs often cannot be differentiated. A carcinoma usually infiltrates into the adjacent structures, giving the lesion a somewhat irregular indistinct contour, but a reactivated tuberculoma may have a similar irregular outline. Carcinoma, for the most part, appears to be homogeneous, while a tuberculoma often shows an inhomogeneous uneven structure, demonstrable particularly by lamina-graphic studies. The differential diagnosis cannot be made by means of bronchography. Abrupt termination of the smaller bronchial ramifications is present in both lesions. The Papanicolaou test of the sputum is decisive if positive but is of no value if negative. Direct aspiration of the tumor should not be done on account of the danger of propagation.

Collapse therapy is useless. If the presence of a

malignant tumor can be excluded with a fair degree of probability, conservative treatment and observation may be tried. However, if there is doubt about the diagnosis, operation is indicated. Lobectomy is being done more and more, not only because it definitely establishes the diagnosis, but particularly because the end-results in the presence of a tuberculoma are remarkably good. The author's 5 patients all made a good recovery.

Five roentgenograms; 1 table.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**Bronchogenic Carcinoma in San Diego County. Relation of Mortality Rates to Findings in Mass Chest X-Ray Survey.** A. S. Churchill. *California Med.* 78: 232-235, March 1953.

A mass chest survey (on 70-mm. film) of some 239,000 persons, representing nearly half the population of San Diego County, California, was analyzed in relation to the mortality from bronchogenic carcinoma.

The disease was correctly diagnosed in 20 persons, of whom 17 died. Twenty-four others in whom it was not detected on survey films died of bronchogenic carcinoma in the following two years. Of the 20 cases found, 16 were in men, all more than fifty-four years of age. Twenty of the 24 cases classified as negative were also in men, the youngest being forty years of age. On review, films of the latter group were again found to be negative in the majority of cases, although at least 6 persons should have been recalled for 14 by 17-inch films. The average time from screening to onset of symptoms in this undetected group was nine months. As only 10 per cent of persons with bronchogenic carcinoma can be cured after onset of symptoms, it is apparent that an interval of one year between survey films is too long.

Examination of all men more than forty years of age every six months should be considered.

Four tables. C. M. GREENWALD, M.D.  
Cleveland Clinic

**The Clinical Significance of Cavernalithiasis.** Denton A. Cooley. *J. Thoracic Surg.* 25: 246-255, March 1953.

Reports dealing with pneumoliths or pulmonary calculi are concerned primarily with the broncholith. Another type of pneumolith, located within the lumen of a pulmonary cavity, may be termed a cavernalith. Like broncholiths, cavernaliths probably arise from partially calcified tuberculous foci. When the caseous material in such a partially calcified focus discharges into the communicating bronchus, the lesion excavates and the larger fragments of calcium remain as calculi within the resulting cavity.

For the most part the cavernalith is a "silent stone." It may, however, produce symptoms either by local trauma and irritation of the pulmonary parenchyma (severe cough, hemoptysis, etc.) or by interference with drainage of the cavity (fever, malaise, pleuritic pain, etc.).

The diagnosis usually depends on the roentgen findings. The presence of calcification in the peripheral lung fields in the neighborhood of a cavity should arouse suspicion that the calcium is within a cavity. The precise diagnosis is dependent upon a change of position of the calcified material as demonstrated on



serial films. Ordinarily the cavernoliths occupy a dependent position in the cavity in any position. Therefore, films made with the patient recumbent, as well as erect, may assist in demonstrating migration of the fragment. The most valuable technic for demonstrating the cavernolith is laminagraphy.

Inert substances lying in infected spaces anywhere in the body interfere with natural healing processes, and in none of the 6 cases of cavernolithiasis reported by the author did spontaneous healing of a cavity occur. In one case a piece of calculus was expectorated, but several larger fragments remained in the cavity. It may be concluded, therefore, that surgical removal of the lesion is the logical means of obtaining a cure. Pulmonary collapse, including pneumothorax, thoracoplasty and plombage, is theoretically unsound in cavernolithiasis.

Twelve roentgenograms; 2 photographs.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Routine X-Ray Examination of the Chest at an Antenatal Clinic.** Audrey Freeth. *Lancet* 1: 287-288, Feb. 7, 1953.

Five hundred and seventy-six women attending an antenatal clinic in a working class area in Glasgow, where tuberculosis was known to be common, were asked to report for x-ray examination, and 541 (94 per cent) responded. Only 1 of this group had known tuberculosis at the time. Evidence of tuberculosis was found in 29 patients (5.3 per cent), and in 4 (0.74 per cent) the disease was definitely active. Another 8 patients had inactive disease but after confinement 2 of them showed definite activity and 2 possible activity. Of the remainder, 4 patients had healed fibrotic lesions and 12 had calcified pulmonary lesions.

The early diagnosis of tuberculosis is particularly vital in pregnancy, as disease discovered in late pregnancy and in the puerperium has a relatively high mortality. One of the various radiological methods of diagnosing pulmonary tuberculosis should be used as a routine antenatal measure.

One table.

**Mobile Floating Fibrin Bulla in the Course of a Hydropneumothorax.** G. Roche, Mme. Houpeau, and M. Odabachian. *J. franç. de méd. et chir. thorac.* 7: 274-279, 1953. (In French)

Therapeutic pneumothorax was initiated in a 48-year-old male with pulmonary tuberculosis. Two months later a serofibrinous exudate appeared. In the upright and both lateral decubitus views a bulla was seen floating on the pleural fluid. Microscopic examination revealed only fibrin. In the discussion Rist mentioned a similar case with several bullae observed by Davy. Mme. Langle stated that she had followed a similar case for seven months, after which the bulla disappeared spontaneously.

Three roentgenograms.

CHARLES M. NICE, M.D.  
University of Minnesota

**Nature and Genesis of Pulmonary Alterations in Carbon Tetrachloride Poisoning.** William Umiker and John Pearce. *Arch. Path.* 55: 203-217, March 1953.

The authors studied the autopsy protocols and microscopic sections from 26 cases of fatal carbon tetra-

chloride poisoning on file at the Armed Forces Institute of Pathology, together with a case from the St. Albans Naval Hospital. Twelve men had been poisoned by ingestion of the chemical and 13 by inhalation of its fumes; in 2 instances the type of exposure could not be ascertained. A history of alcoholism was frequently elicited, and many of the men became ill after a bout of acute alcoholism. Their courses were characterized by clinical and laboratory evidence of liver and kidney failure. The interval between time of exposure and time of death varied from one to sixteen days, with the greatest number of deaths occurring on the tenth day. Hepatic damage predominated in patients who died within the first week, while renal insufficiency with uremia was the most important feature in later fatalities.

The basic lesion consisted of an exudate of fibrin, a pseudomembrane lining the alveolar walls, which were thickened by growing fibroblasts, and a proliferation of cells resembling the alveolar lining epithelium.

Results of roentgen examination of the lungs were recorded in 12 cases. In all but 1, abnormalities were found. The earliest change appeared on the ninth day after exposure, and the incidence of positive findings increased each additional day thereafter. The changes consisted of fluffy hilar opacities of varying density, which on subsequent examinations gradually extended peripherally. In no instance did the lesion quite reach the pleural surface. Widening of the cardiac silhouette was frequently observed, but it could not be ascertained with certainty whether the pulmonary changes preceded or followed the cardiac enlargement.

The appearance of the lungs in 9 cases of rapidly developing uremia from different causes was compared with that in the carbon tetrachloride group and was found to be essentially the same. The roentgenograms of the lungs in the two groups were also similar.

The authors believe that it is highly probable that the pulmonary changes in carbon tetrachloride poisoning are the result of the uremia produced by the necrotizing action of that chemical on the kidney, rather than the result of its direct action on the pulmonary parenchyma during either inhalation or excretion.

One roentgenogram; 13 photomicrographs; 1 photograph; 1 table.

**Clinical Experience with the Water-Soluble Bronchography Compounds.** Mordant E. Peck, Adrian J. Neerken, and Emmanuel Salzman. *J. Thoracic Surg.* 25: 234-245, March 1953.

There are five proprietary water-soluble media for bronchography now available, all of which have as the contrast medium iodopyracet (Diodrast) or a closely related product. The five preparations are Umbradil Viscous B, Per-Abrodil "M," Ioduron B, Diodone Visquese, and Methocel-Diodrast, containing 50 per cent Diodrast and 1.75 per cent methylcellulose.

The authors reviewed 56 bronchograms made with Methocel-Diodrast, of which 66.7 per cent were satisfactory and 33.3 per cent unsatisfactory. One of the authors (A. J. N.) had kept records of 528 bronchograms obtained in the Army with Lipiodol; 83 of these, or 15.9 per cent, were unsatisfactory, which would tend to indicate that better results can be obtained more consistently with one of the non-absorbable iodized oils.

An explanation is offered for the discrepancy between results obtained with the two types of medium.

First, the absorption of iodopyracet is extremely rapid. Second, the material is miscible with the bronchial secretions and tends to fill the peripheral bronchial tree confluent, while with iodized oil "clubbing" due to blockage by retained secretions is observed. Third, and perhaps most significant, is the fact that the water-soluble media tend to create a rather severe degree of bronchospasm, with incomplete filling secondary to the explosive effect of coughing. The elimination of coughing is more difficult to obtain with iodopyracet compounds than with iodized oil, though improvement in this respect will be obtained with meticulous attention to the topical anesthetization of the tracheobronchial mucosa. The authors believe that bronchospasm is somewhat greater with products utilizing carboxymethylcellulose as a base, since the viscosity is so low that the iodopyracet is more rapidly absorbed from the bronchioles and alveoli.

The use of water-soluble media may also carry the risk of a fatality. The authors had two deaths associated with bronchography in which Methocel-Diodrast and Methocel-Urokon were used. It is their opinion that the high molecular carbohydrate base precipitated the fatal anaphylactic reactions.

The concept of a water-soluble agent which will disappear from view shortly after the x-ray examination is especially appealing for tuberculous patients, as well as in routine bronchography. Residual iodized oil is a definite handicap to the future study of the pulmonary tree. The available water-soluble agents are helpful in overcoming this difficulty but they cannot be used without an awareness of the complications and difficulties related to their use. These difficulties might be grouped into three categories: namely technical, toxic, and latent tissue reactions.

It can justly be said that no compound yet available has all the ideal characteristics for a bronchographic medium. The current water-soluble compounds are a step in the right direction but should not preclude further search for a more ideal agent.

Seven roentgenograms. DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Dionosil, Contrast Medium for Bronchography (Report of Our Experiences).** L. Arrieta Sánchez. *Radiologia* 3: 77-80, March 1953.

Dionosil is a British water-insoluble medium used in the form of a 50 per cent aqueous suspension. Animal experiments with incorporated radioactive iodine have shown that the compound is absorbed after hydrolysis but all the iodine remains in organic form. The medium does not disperse in the alveoli even with the use of excessive quantities. Unlike Lipiodol, which fills the bronchus, Dionosil tends to spread thinly along the bronchial wall; the author has even observed this mucosal coating to spread to bronchi other than those studied. A clear, detailed, delicate mucosal outline results (a "bronchomucosogram").

The rapidity of absorption is proportional to the dose used. Tests showed that 15 c.c. was adequate for outlining the bronchial tree of one lung, and this dose was usually absorbed within 120 hours. This rate of absorption avoids the inconveniently short period within which films have to be exposed when water-soluble media are used; on the other hand, within a few days absorption is so complete that no trace can be detected on the chest films.

The same methods of anesthesia may be used as with other media, but anesthesia need not be so complete. No side effects, such as dyspnea, anaphylactic reactions, nausea, or vomiting, were observed; cough was slight, if present at all.

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**Could a Damaged Liver Be the Cause of a Lethal Pantocain Intoxication?** H. Fietz. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 336-341, March 1953. (In German)

Since the introduction of the water-soluble contrast media for the visualization of the tracheobronchial tree, the problem of anesthesia of the mucous membranes has assumed a new aspect. These media are quite irritant due to their hypertonicity, and the anesthesia has to be extended almost to the alveoli. This requires a much larger quantity of the anesthetizing agent. Furthermore, resorption of the anesthetic becomes more rapid as the alveoli are approached. In the alveoli, the resorption is almost equivalent to an intravenous injection, as the membrane separating them from the capillaries is less than a micron in thickness.

The author reports the death of a 52-year-old patient in whom bronchography was done to establish the diagnosis of a lesion in the right upper lobe. The patient had lost a great deal of weight, his sclerae were slightly icteric, he was short of breath and had bronchitic râles over both lungs. A roentgenogram showed an infiltrative process with a large cavity in the right infraclavicular area. The general examination revealed marked enlargement of the liver, its lower border being 4 fingers below the costal margin. Bronchography, under Pantocaine anesthesia, showed an occlusion of the right upper lobe bronchus. On the basis of the x-ray examination, a diagnosis of bronchogenic carcinoma of the right upper lobe, with central necrosis, was made.

Immediately following bronchography, the patient became quite restless and epileptiform convulsions developed, first in the upper extremities and then extending over the entire body. At the same time, there was a marked shortness of breath. Attempts to control the convulsions were unavailing, and death ensued. It was attributed to Pantocain intoxication.

Anesthesia was obtained in the following manner: Two cubic centimeters of a 1 per cent solution of Pantocain was first sprayed into the larynx. With a curved syringe another 2 c.c. was administered to the larynx and the trachea. For the intrabronchial anesthesia 5 c.c. of a mixture of a 0.5 per cent solution of Pantocain and 0.5 per cent Salicain was used. No adrenalin was given. The time of administration of the anesthesia was between twelve and fifteen minutes. It is assumed that half of the anesthetic may have been eliminated by expectoration. The author believes that perhaps 35 mg. of Pantocain and 5 mg. of Salicain may have been resorbed by the patient. This quantity is below the presumed minimal lethal dose, which is said to be 60 mg.

According to various authors, the toxic action of Pantocain is not so much dependent upon the absolute quantity of the anesthetic as upon the concentration within the blood at any given time. The latter depends upon the concentration and quantity of the anesthetic used, the rate of resorption, the time of administration, the resistance of the patient, and, to a

great extent, upon the detoxicating action of the liver. Postmortem examination of the author's patient showed a definite cirrhosis of the liver but no carcinoma metastases. Death is attributed to the advanced liver damage and consequent failure of detoxification of the Pantocaine.

The question of the addition of adrenalin to the anesthetic seems to be still unsettled. Some authors believe that adrenalin causes a constriction of the vessels and therefore delays resorption; others believe that adrenalin adds to the toxic action of the anesthetic.

In conclusion, it may be said that, in the use of Pantocaine as a mucous membrane anesthetic preparatory to bronchography, caution should be exercised. The quantity should be kept to a minimum, application should be made slowly, and patients with advanced liver damage should probably not have this type of examination.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**The Marginal Shadow Sign of the Heart.** H. Eck. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 313-316, March 1953. (In German)

The heart, being a dense, solid organ, should show on an x-ray film sharply outlined right and left lateral borders against the partially translucent air-containing lungs. A survey of many routine chest films has shown that occasionally the margin of the heart is indistinct and blurry, more often on the right side but sometimes also on the left. This phenomenon has been given the name *Schattenrandzeichen am Herzen*, which is probably best translated as "marginal shadow sign of the heart." The lung structure adjacent to the blurry area of the heart is often slightly thickened.

Formerly, it was believed that this shadow was caused by a pleuritic effusion in the interlobar space. More recent investigations have shown that the phenomenon is due for the most part to an infiltration of the medial portion of the middle lobe if found on the right side, and of the lingula of the left lower lobe if found on the left side. If a postero-anterior view of the chest is taken in hyperlordosis, the cleft between the right upper lobe and the middle lobe and that between the right middle lobe and the lower lobe are projected tangentially. The right middle lobe then appears as a triangle, the base of which is directed toward the lateral surface of the chest wall while the apex is in the hilus area. If such a film is obtained in cases with a marginal shadow sign of the heart, it can be seen that the shadow is confined to the middle lobe and is sharply demarcated by the two clefts of that lobe. The apex of the triangle appears to be blunted. In the left lung, this area corresponds to the lingula. The previous conception that the shadow was caused by an interlobar effusion can easily be disproved by a lateral view of the chest.

The marginal shadow sign on the right side is due usually to old tuberculous involvement; on the left side, the most common cause is a recent reversible virus infection.

Four roentgenograms.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**Loculated Azygos Fissure Effusion in Cardiac Failure.** Robert L. Friedman. *Ann. Int. Med.* 38: 582-585, March 1953.

The author reports what he believes to be the third

case of loculated azygos fissure effusion in the literature. The patient had previously undergone a surgical procedure for decortication of the lung, which had probably produced fibrous adhesions that obliterated the pleural space. Cardiac failure subsequently developed, and a loculated effusion in the azygos fissure was noted on the roentgenograms. This accumulation of fluid disappeared after the patient showed clinical improvement from the cardiac condition.

Three roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**The Pulmonary Circulation in the Diagnosis of Congenital Heart Disease.** Sumner N. Marder, William B. Seaman, and Hugh M. Wilson. *J. Thoracic Surg.* 25: 305-315, March 1953.

In a series of cases of congenital heart disease, the clinical and conventional radiographic findings were correlated with data furnished subsequently by angiocardiology, cardiac catheterization, operation, and autopsy. The outstanding conclusion of this study was that accurate evaluation of the pulmonary circulation is the single most important contribution of the conventional examination. When the caliber of the pulmonary arterial tree provided unequivocal evidence of either increased or decreased pulmonary blood flow, it was rarely necessary to undertake specialized diagnostic procedures. A competent clinical history, physical examination, conventional roentgenograms, and unipolar electrocardiograms provide all the essential information in the majority of patients.

It has been shown that increased pulsations and increased caliber of the pulmonary vessels indicate either increased blood flow, increased blood pressure, or both. The congenital cardiac anomalies which may exhibit these findings are many and embrace all categories—acyanotic, cyanotic, and cyanose tardive. In the group in which there is increased pulmonary blood flow and/or pulmonary hypertension, the main challenge will be to separate the atypical cases of patent ductus from such lesions as septal defects. In general, unipolar electrocardiography will be of greater value than roentgenography for this purpose. However, in some instances obvious cardiac enlargement with a negative electrocardiogram may be encountered as a result of pulmonary hypertension of such degree as to cause right, as well as left, ventricular enlargement. In such cases, fluoroscopic observation of an active and prominent aorta and the finding of an enlarged left auricle on barium swallow may be of value.

Pulmonic stenosis, with pulmonary hypotension, will be observed in the majority of cyanotic lesions for which surgical attack is feasible. From the practical point of view, four anomalies must be considered in this group—the tetralogy of Fallot, pulmonic stenosis with atrial septal defect, isolated (pure) pulmonic stenosis (with intact septa), and tricuspid atresia with pulmonic stenosis.

If the diagnosis of pulmonic stenosis be established, consideration of heart size and the frequent association of valvular stenosis with poststenotic dilatation of the pulmonary artery will allow further differentiation. In general, the tetralogy of Fallot will show a normal or slightly enlarged heart without evidence of poststenotic dilatation of the pulmonary artery. Slight or moderate cardiac enlargement with poststenotic pulmonary

artery dilatation is characteristic of cases of pulmonic stenosis with atrial septal defect. Pulmonic stenosis with considerable cardiac enlargement (usually obscuring the poststenotic dilatation of the pulmonary artery) suggests an isolated pulmonic stenosis.

Ten roentgenograms; 2 tables.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**A Method of Angiocardiography.** Ian M. Hill. Brit. J. Surg. 40: 444-446, March 1953.

The author describes a method of angiocardiography used in 120 cases, with precautions to reduce to a minimum the mortality which may be expected in the investigation of serious cases of congenital heart disease. In this series 3 deaths occurred, and there was one instance of cerebral damage secondary to anoxia.

Before the procedure is performed, careful evaluation of the physical findings and history is undertaken. A history of attacks of unconsciousness is particularly indicative of a high risk. For children under ten a general anesthetic is used; for adults local analgesia is sufficient. Oral tests for sensitivity to Diodone precede the examination. The importance of having a trained anesthetist and a supply of oxygen readily available is stressed.

Under aseptic precautions the basilic or cephalic vein of either arm, or the external jugular vein in children, is exposed and cannulated. Attached to the cannula is a 3-way blood transfusion syringe. When the patient's condition is considered stable, a trial injection of 10 c.c. is given to estimate the freedom of vein flow. Initially normal saline was used for this purpose; more recently this has been replaced by 0.2 per cent procaine solution in isotonic glucose. Evidence of cardiac irritability calls for further intravenous procaine before injection of the contrast medium. The syringe is then emptied and filled with the desired volume of 70 per cent aqueous Diodone solution. The factors to be considered in determining the dosage are: age, size, weight, size of the chest, degree of disability, and type of cardiac lesion. In the series reported the amount ranged from 25 c.c. in a severely disabled child of four years to 80 c.c. for a large adult. Whatever the dosage, the injection should be completed in less than two seconds, preferably a second and a half. The first exposure is made as the plunger moves down the syringe. On completion of the injection, the vein is flushed with procaine-glucose solution to remove the Diodone and thus lessen the possibility of thrombosis.

Oxygen is administered until the heart beat is normal. A syringe containing adrenalin solution and equipped with a long needle is kept available for percutaneous left ventricular puncture in the event of cardiac arrest.

One photograph. J. L. CLEMENTS, JR., M.D.  
Atlanta, Ga.

**The Role of the Exposure Rate in Angiocardiography.** Carl Wegelius and John Lind. Acta radiol. 39: 177-191, March 1953.

The authors discuss the influence of the exposure rate in angiocardiography and state that, from their analysis, it would appear that the present standard method, with a slow rate of exposure, will as a rule offer satisfactory anatomic information on the inner morphology of the heart and the great vessels, provided no mal-

formations, demonstrable only as rapid transitory phenomena, are present. In order to assess the dynamic action of the heart at all frequencies, a rate of 10 to 12 exposures per second is necessary. The relative merits of the "anatomic" and "dynamic" methods of examination are pointed out. The latter, incorporating simultaneous electrocardiography and automatic exposure marking, correlates all the information given by the former with the more physiologic aspects of the heart mechanism.

Forty-five roentgenograms.

A. J. NICHOLAS, M.D.  
Shreveport, La.

## THE DIGESTIVE SYSTEM

**Duplications of the Alimentary Tract in Adults, with a Report of Three Cases.** John J. Nolan and J. Gordon Lee. Ann. Surg. 137: 342-348, March 1953.

Alimentary tract duplications are congenital anomalies that may occur anywhere from the oral cavity to the rectum, being found most commonly in relation to the ileum. There are two types: *spherical*, which has been variously described in the past as enterogenous cysts, gastric cysts of the esophagus, enterocystomas, and inclusion cysts of the alimentary tract; *tubular*, frequently mistaken for unusual Meckel's diverticula.

The duplication may be in communication with the parent hollow viscus or may lie apart from it. The walls are thick and muscular, and the duplication and the normal alimentary tract have a common muscularis. The mucosa differs from the normal gut wall, as heterotopia is the rule.

Alimentary tract duplications are to be distinguished from mesenteric cysts, which are of lymphatic origin, and from Meckel's diverticula, which arise from failure of the vitello-intestinal duct to regress. Gastric diverticula of the congenital type are probably closely related to duplications. Clinically, the duplication usually produces symptoms early in life. Volvulus, intussusception, carcinomatous degeneration, attainment of a remarkable size, location in a hernia sac, and incidental detection on a chest roentgenogram have been described.

The authors report 3 cases of duplication in adults: (1) a massive gastric duplication associated with hemorrhage; (2) a spherical duplication of the esophagus associated with inferior vena caval compression; (3) a spherical duplication of the ileum associated with intussusception.

Esophageal duplications are often diagnosed roentgenologically, before symptoms are produced. The spherical type is said usually to project into the right lung field; the tubular type, as a rule, fills with barium. Gastric abnormalities have been detected on x-ray examination in duplications of the stomach, but correct interpretation prior to operation has not been reported. Small bowel duplications, unless they are tubular or very large, are difficult to recognize. Cecal or colonic lesions are more favorable for study.

In the surgical treatment, the two important points to be considered: (1) the common muscularis between the duplication and the parent gut, so that no plane of cleavage can be established; (2) the fact that the blood supply of the normal intestine may be destroyed by removal of the duplication. For these reasons, removal of both the normal and abnormal alimentary tract is the method of choice. If the organ concerned



has a large lumen and an almost indestructible blood supply, like the stomach, resection may be done, with closure of the resultant defect. Small spherical duplications may be removed by simple excision.

A total of 19 alimentary tract duplications have been reported, including the 3 described by the authors. Acceptance of standard nomenclature for these anomalies will probably result in an increase in their recognition in adults.

Five roentgenograms, 1 photograph.

SEYMOUR A. KAUFMAN, M.D.  
Boston, Mass.

**Foreign Bodies and Roentgen Examination of Perforation of the Esophagus.** Eelco Heizinga. *Ann. Otol. Rhin. & Laryng.* 62: 107-113, March 1953.

The principal indication for external operation for a foreign body in the esophagus is the occurrence of peri-esophagitis. In such cases, x-ray examination by means of lateral views of the neck is of the greatest importance. On the lateral film, the inflammatory reaction, with edema and swelling, is manifest as a widening of the tissue shadow between the spine and trachea. Still more important is the demonstration of air between the trachea and spine, which may indicate perforation of the esophagus. The presence of a few small air bubbles may not be significant. A large air bubble, on the other hand, may represent an abscess either in the esophageal wall or the peri-esophageal tissues. Finally, emphysema of the interstitial tissues of the neck is a definite sign of perforation. It is demonstrable in a lateral view as a light streak in front of the spine, sometimes reaching as high as the nasopharyngeal cavity. Esophageal perforation is not of itself considered an indication for operation. The circumstances of the individual case are the deciding factor. A number of roentgenograms of patients seen with large peri-esophageal abscesses and perforations of the esophagus successfully treated by external operation are reproduced.

Four roentgenograms. STEPHEN N. TAGER, M.D.  
EVANSVILLE, IND.

**Curling of the Esophagus.** Marshall Eskridge and John Day Peake. *South M. J.* 46: 213-220, March 1953.

The authors present 18 cases of curling of the esophagus observed in a series of 2,295 patients of all ages in whom the esophagus was observed fluoroscopically for various reasons. A nineteenth case from another hospital is added to illustrate the serious possibilities of the condition.

Curling is a descriptive term and has nothing to do with etiology or pathology. Radiographs of the esophagus made at the correct moment show a corkscrew or coiled effect. Fluoroscopically, following a barium swallow, one sees in the unobstructed cases a sudden appearance of varying numbers of ring-shaped constrictions that may completely occlude the lumen and do not move up or down. This is usually before the first wave of peristalsis; when that arrives, the portion above the tight constriction distends until some of the barium is regurgitated above the peristaltic wave. In some patients diverticula appear. The peristaltic wave is entirely independent of the constricted areas and passes down to the cardia. The constriction then gradually relaxes and the esophagus distends to a larger

than average size. If the patient swallows again, the whole cycle is repeated. In some it appears to occur spontaneously, with a regular cycle of contraction and relaxation. In the most severe cases there is so little relaxation that gastrostomy may be necessary to keep the patient from starving.

The etiology is obscure. In experimental animals spasm of the distal end of the esophagus has been produced by pharyngeal stimulation, stimulation of the sciatic nerve, traction on the vagus nerves, sudden stretching of the stomach, strong distention of the urinary bladder, large or small intestine, and various types of mechanical stimulation of the gallbladder, common bile duct and skin. Numerous authors have noted the association of curling with various diseases such as gastric ulcer or carcinoma, hiatus hernia, duodenal ulcer, coronary disease, parkinsonism, etc. All seem to agree that it typically occurs in nervous, high-strung individuals over the age of fifty, who usually have a pathologic condition elsewhere. The gist of research and clinical experience points to a reflex origin, with stimulation by organic disease or psychic factors.

Roentgenologically the condition is usually easily recognized, but associated disease of the esophagus must be ruled out, notably carcinoma. In cases of complete obstruction this may sometimes be impossible. Treatment is generally not very satisfactory for symptomatic cases.

The authors' 19 cases are briefly reported. Seven were symptomatic. Eleven patients were over sixty-five years of age and 9 over seventy. Complicating disease was common, with cardiac disease most frequent.

Fourteen roentgenograms; 1 table.

JOHN M. KOHL, M.D.  
Jefferson Medical College

**Dysphagia Produced by a Contractile Ring in the Lower Esophagus.** Franz J. Ingelfinger and Philip Kramer. *Gastroenterology* 23: 419-430, March 1953.

The authors describe 6 cases, all in males, characterized by sudden attacks of dysphagia recurring intermittently over a variable period of time. The dysphagia was described as a painful sticking sensation quite sharply localized under the lower portion of the sternum. The attacks occurred only during eating, and the patients had no doubt that a portion of the offending food became stuck in the esophagus. The distress ranged in intensity from moderately severe to agonizing and was at times accompanied by considerable anxiety. The attacks varied in frequency with the severity of the esophageal disorder. In most instances they were precipitated only by certain types of food or hasty swallowing without proper mastication. Because the symptoms were intermittent, progressive weight loss and debility were not present. Regurgitation between attacks and prolonged substernal burning did not occur.

The radiologic appearance of the constriction following a swallow of barium was qualitatively identical in all 6 cases. The degree to which the esophageal lumen was narrowed varied, however, not only from patient to patient but also in the same individual. At the point of its maximal development, the constriction consisted of a sharply demarcated negative shadow, a ring-like band, 2 to 6 mm. in width, intersecting the lumen at a right angle to the long axis of the esophagus. The constriction was not funnel-shaped but tended to

form a clearly defined angle with the esophageal wall. Total occlusion of the esophagus did not occur, but in the more severe cases only a thin line of barium identified the residual lumen in the constricted area. The location of the constriction was 2.5 to 6 cm. above the junction of the esophagus and stomach. Its anatomical relationship to the diaphragm was less constant but the annular narrowing usually appeared 0.5 to 2.5 cm. above the shadow cast by this structure.

In the milder cases, the constriction was not always visible as the initial portion of barium reached the lower esophagus. As the principal mass of the medium, propelled by a primary peristaltic wave, distended the lower esophagus, the annular indentation made its appearance, becoming more pronounced as the peristaltic wave approached. Once the esophagus had emptied itself, the ring could no longer be seen.

There was no evidence of retarded esophageal emptying or of dilatation of the esophagus proximal to the contractile ring, except when the patient was given solid food along with the barium mixture. Under these circumstances, as peristalsis pushed the bolus into the lower esophagus, the constricting ring narrowed down upon the solid material, plugging the small lumen at the center of the contraction, with transient dilatation proximally.

Esophagoscopy, performed in 3 of the 6 patients, showed no abnormality. One patient was treated by surgical resection of the distal 4 cm. of the esophagus. Another received marked benefit from dilatation of the lower esophagus. The other patients have been essentially asymptomatic following conservative measures, including full mastication of solid foods.

The mechanism and pathogenesis of this syndrome and its relationship to cardiospasm or achalasia are discussed.

Thirteen roentgenograms; 1 photomicrograph; 1 table.

RICHARD A. ELMER, M.D.  
Atlanta, Ga.

**Pneumoperitoneum in the Radiologic Diagnosis of Cardial and Paracardial Tumors of the Stomach.**  
Carlo Meneghini and Renato de Marchi. *Radiol. clin.* 22: 97-118, March 1953. (In Italian)

While diagnostic pneumoperitoneum has been used before in the diagnosis of tumors in the region of the cardia, the authors have seen fit to describe their experiences with this method in 7 cases, since all were subjected to surgery and accurate correlation could be made between the radiographic and the operative findings.

The method is essentially one of double contrast; the interior contour of the stomach is made visible by a barium suspension, and the outside contour by the pneumoperitoneum. Between one and one-half liters of oxygen was used. Upright fluoroscopy gave the most information. In contrast to the routine barium examination of the stomach, the combined method demonstrated the extent, shape and volume of the tumor and the presence of adhesions between the tumor and surrounding structures, especially the diaphragm, thus serving as a basis for the preoperative estimate of operability, the method of approach, etc. Study of the 7 cases showed clearly how the findings on routine barium studies were amplified and clarified by pneumoperitoneum, and how well these findings corresponded with the actual conditions at operation.

The authors emphasize the importance of this method in excluding early lesions in the region of the cardia when routine barium studies suggest their presence.

Most of the 11 roentgenograms are accompanied by line drawings clearly illustrating the findings.

CHRISTIAN V. CIMMINGO, M.D.  
Fredericksburg, Va.

**Crohn's Disease Involving the Stomach. A Report on Two Cases.** F. R. R. Martin and R. J. Carr. *Brit. M. J.* 1: 700-702, March 28, 1953.

Crohn has described three main varieties of the disease which bears his name: ileitis, ileojejunitis, and ileocolitis. He has also mentioned cases in which the second and third parts of the duodenum were involved, with radiologic appearances suggesting spread of the disease to the stomach (see Crohn, Burrill: *Regional Ileitis*. New York, Grune & Stratton, 1949. Reviewed in *Radiology* 53: 431, 1949).

The authors report two cases, both in young women, with involvement of the stomach and duodenum in association with inflammatory disease of the ileum and proximal colon. Both patients complained of abdominal pain, loss of appetite, and fairly persistent vomiting.

In one patient, at the time of the initial roentgen demonstration of the gastric and duodenal lesions, no inflammatory process involving the ileum or cecum was present. The original films, reproduced here, show the absence of mucosal folds in the antrum, cap, and upper half of the descending part of the duodenum. There is a sharp demarcation between the pathological and normal segments of the stomach and duodenum. Above and below the involved area, the mucosal relief pattern was normal. Three months later early changes in the mucosal pattern of the terminal ileum were demonstrable. At the time of abdominal exploration, typical changes of Crohn's disease were found in the terminal ileum, and irregular inflamed patches were present throughout the colon. The stomach wall appeared to be only a little thickened, but in view of the roentgenologic findings, biopsy was done. The report read as follows: "The stroma is heavily infiltrated by lymphocytes, plasma cells, and endothelial cells. Giant cells are present. No caseation or tubercle bacilli were found. A chronic granulomatous process like Crohn's disease appears to be present."

The second patient had a resection of the terminal ileum and right side of the colon for what appeared to be localized disease. Approximately six months after operation she experienced abdominal pain, anorexia, and repeated vomiting, and at this time typical radiographic changes were present in the stomach and duodenum.

The authors stress the point that when persistent anorexia and vomiting occur in a patient with regional ileitis, ileojejunitis, or ileocolitis, in the absence of other clinical evidence of intestinal obstruction, the possibility of involvement of the stomach and duodenum in the pathological process would be considered. Having seen 2 cases in the period of eighteen months, they believe that there may be a considerably greater incidence of gastric and duodenal involvement than has been recognized.

Four roentgenograms.

RICHARD A. ELMER, M.D.  
Atlanta, Ga.

**Permanent Deposition of Iodine Contrast Medium in the Wall of the Stomach.** Albert Bogsch. *Acta radiol.* 39: 219-224, March 1953.

The author reports a case in which certain opaque substances were seen in the wall of the stomach during a gastrointestinal study with a barium meal. At autopsy this opaque material proved to have arisen from an iodine contrast medium deposited on the occasion of cholecystography some three years previously, prior to removal of stones from the common duct and cholecystectomy. The following explanation for penetration of the medium into the submucosa of the stomach is offered:

"Cicatrized adhesions, found subhepatically, were doubtlessly the result of repeated inflammation around the gallbladder. The cystic and common bile ducts were markedly distended by stones, and were embedded tightly in the surrounding connective tissue. Lymph ducts had grown into this tissue, which owing to the position of the adhesions ran to the nearest part of the stomach, *i.e.*, to the region of the antrum and pylorus. When contrast medium was introduced into the gallbladder and ducts, and the presence of stones prevented its evacuation, it filled the lymph vessels leading to the stomach wall. The thin-walled, easily distensible lymph ducts became occluded as a result of inflammation, and the contrast medium remained deposited for a protracted period, to be disclosed three years later on roentgen examination."

Four roentgenograms; 4 photographs and photomicrographs.

A. WILSON BROWN, M.D.  
Shreveport, La.

**Pyloric Obstruction Due to Mucosal Diaphragm.** Alexander N. Rota. *Arch. Path.* 55: 223-226, March 1953.

A case is presented of intermittent obstruction due to a mucosal diaphragm with a small central opening, situated at the pylorus, in a woman of seventy-four years. The patient had complained of intermittent attacks of nausea and vomiting followed by diarrhea over a period of eight years. She had sought medical advice on several occasions, and roentgen studies had been made in 1942 and 1944. The first report was "pyloric ulcer with partial obstruction," and the second was "pyloric obstruction with 25 per cent retention in twenty-four hours; thickening of the pylorus due to either scirrhus carcinoma or scar tissue of healed ulcer." The patient received various forms of medical treatment without obtaining much relief. She was seen by the author in 1951. Physical examination showed nothing of significance. Laboratory studies were within normal limits. Repeated barium series revealed only an "atonic and ptosed stomach with no evidence of ulcer or new growth in the stomach or duodenum." A partial gastrectomy was performed. Thirteen months later the patient had gained weight and was free of symptoms.

Examination of the specimen removed at operation showed that the pyloric musculature was thickened into a firm but wide ring. A finger inserted into the pylorus did not pass through but demonstrated the presence of a mucosal diaphragm. When the diaphragm was pushed into the stomach and the stomach was then everted over the finger, a small opening approximately 0.4 cm. in diameter was discovered in the center of the diaphragm. The diaphragm appeared

to be formed of a circumferential fold of redundant mucosa. The duodenal mucosa was not remarkable. The pathogenesis of the lesion could not be established with certainty.

The authors found only 2 other cases of pyloric obstruction by a mucosal diaphragm recorded in the medical literature (Touroff and Sussman: *Surgery* 8: 739, 1940; Sames: *Brit. J. Surg.* 37: 244, 1949. *Abst. in Radiology* 55: 300, 1950). In these cases the obstruction was prepyloric in position. [A case of partial gastric atresia due to a prepyloric mucosal diaphragm, probably of congenital origin, was reported by Gross and Durham in the September 1953 issue of *RADIOLOGY* (61: 368, 1953)].

Two photographs.

**Benign Prolapse of Gastric Mucosa. Clinical, Roentgenologic, and Gastroscopic Study.** Jacob Lichstein and Leonard M. Asher. *J.A.M.A.* 151: 720-724, Feb. 28, 1953.

The authors report on a series of 52 patients in whom the primary diagnosis was prolapse of redundant mucosa through the pylorus. Seventy-five per cent of the group were between the ages of forty and seventy. Of 45 patients for whom a history was available, 38 had symptomatic complaints. There was no clear-cut symptom complex, the symptoms being indistinguishable from those of other functional digestive conditions. The most frequent complaints were repeated bouts of localized epigastric pain, often associated with nausea and vomiting and not relieved by food. These acute cramping episodes, sometimes lasting for several days, appeared in 31 per cent of the cases. There was a high incidence of hemorrhage of varying degree (22 per cent). A significant observation was the finding of coexisting gastrointestinal disease. Thirty-eight per cent of the patients had peptic ulcer, either duodenal or gastric; 38 per cent had various types of gallbladder disease.

At present, the diagnosis of gastric mucosal prolapse is made solely on the basis of the roentgenologic study. The defect is confined to the base of the bulb. It is smooth in contour, is lobulated like an umbrella, and is "mushroom" in outline. The gastric rugae are seen passing from the antrum transpylorically into the bulb. The remainder of the bulb is usually completely filled out in the absence of a true duodenal ulcer.

Forty-five gastroscopic examinations were performed on 37 of the patients. Redundant mucosal folds were seen in 40 per cent of the 37, hypertrophic gastritis in 34.8 per cent, and superficial gastritis in 20 per cent; in 9 cases the phenomenon of the prolapsing mucosa was visualized during the examination.

The indications for surgical intervention are about the same as those for ulcer: (1) intractability to conservative treatment, with persistence of pain, (2) pyloric obstruction, (3) recurrent hemorrhage, and (4) the possibility of the presence of a prepyloric malignant growth.

In concluding, the authors state that it is difficult to prove that gastric mucosal prolapse is a definite clinical entity. This is particularly true since there was a relatively high incidence of neuropsychiatric stigmata in their group of patients. The high incidence of gastrointestinal disease was certainly also significant.

Four roentgenograms; 1 drawing.

ALFRED O. MILLER, M.D.  
Louisville, Ky.

**Transpyloric Prolapse of Gastric Mucosa.** W. P. Kleitsch and R. L. Lawton. *Am. J. Digest. Dis.* 20: 67-71, March 1953.

Transpyloric prolapse of gastric mucosa can be a source of symptoms in at least some cases. The clinical picture is that of chronic gastritis with superimposed inconstant obstruction. The radiological appearance varies with the amount of mucosa prolapsed and the degree of obstruction.

Three different x-ray pictures are described: (1) moderate prolapse through a relatively normal pylorus, producing a filling defect in the base of the bulb, the "umbrella" or "toadstool" sign; (2) complete filling of the pyloric canal by mucosa with non-visualization of the bulb and pinching of the pyloric antrum, giving a "funnel" sign; (3) compensatory dilatation of the pyloric canal resulting in a relatively large amount of mucosal prolapse, with the rugal pattern extending into the base of the bulb.

Even at laparotomy it is possible for the surgeon to overlook the condition. Palpation is inconclusive and gastrotomy may be needed for confirmation of the diagnosis.

Three cases are presented with the diagnosis of prolapsed mucosa made only at operation, surgery having been performed due to confusion of the x-ray findings with carcinoma. A correct x-ray interpretation was made only in retrospect.

Treatment should be kept as simple as possible. A trial of medical management should precede laparotomy. Mutilating operations are to be avoided. A procedure such as the Heineke-Mikulicz pyloroplasty is considered adequate.

Three roentgenograms; 2 photomicrographs; 1 photograph.  
C. M. GREENWALD, M.D.  
Cleveland Clinic

**An Understanding of Prolapsed Gastric Mucosa.** Francis W. Wilson. *Am. J. Digest. Dis.* 20: 71-72, March 1953.

A concise discussion of the controversial subject of prolapsed gastric mucosa is presented. Causes are undoubtedly multiple. Gastric hyperperistalsis is a constant feature, and may be either primary, preceding prolapse and aggravating it, or a secondary compensatory mechanism. Herniation may be reducible or irreducible. To consider prolapsed mucosa physiological is, in the author's opinion, the equivalent of considering an inguinal hernia physiological.

Symptomatology is understandably vague and inconstant. Because of this, roentgenology remains the only non-surgical method of diagnosis, and rigid criteria must be observed. These are listed as follows: (1) hypermotility of the stomach; (2) characteristic deformity of the duodenal bulb; (3) ability to trace elongated gastric folds into the deformity of the base of the bulb; (4) absence of a "quick" duodenal bulb. Failure to adhere to these criteria is probably the greatest factor in the variation in incidence, and in percentage of asymptomatic cases, reported by different authors.

Therapy is directed along physiological lines, including antispasmodics, soft or liquid diet, and antacids. A few patients require surgical intervention. The indications for surgery are obstruction, recurrent bleeding, and intractable pain.

C. M. GREENWALD, M.D.  
Cleveland Clinic

**Leiomyosarcoma of the Duodenum. Report of a Case and Summary of the Literature.** Mandel Weinstein and Morton Roberts. *Arch. Surg.* 66: 318-328, March 1953.

Leiomyosarcoma is the rarest tumor occurring in the duodenum, only 27 cases having been reported previously. The authors describe a 28th case.

The tumor grows slowly, ulcerating the duodenal mucosa and invading the surrounding structures, *i.e.*, the pancreas, colon, mesenteric vessels, and kidney. It may attain a large size and metastasizes both locally and diffusely through the body. The usual symptoms are weight loss, weakness, anemia, and abdominal pain. Usually there has been some blood in the stools. Roentgen examination may reveal pressure defects or a barium-filled cavity if the tumor ulcerates and empties into the lumen of the intestine. The prognosis is poor because of the difficulty of surgical removal, due to the extent of invasion and the possibility of a breakdown of the anastomosis and postoperative fistula formation.

One roentgenogram; 1 photomicrograph; 2 drawings; 1 table summarizing the reported cases.

PAUL MASSIK, M.D.  
Quincy, Mass.

**Intestinal Obstruction Resulting from Biliary Calculi (Gallstone Ileus).** Samuel Shore, Harry H. Jacob, and Jack A. Cannon. *Arch. Surg.* 66: 301-311, March 1953.

The authors describe and discuss 7 cases of gallstone ileus (in 6 patients), comprising 5 per cent of 136 instances of intestinal obstruction seen in a three-year period. Calculi entering the intestine through a fistulous communication with the gallbladder are usually passed *via* the rectum but may become impacted and cause acute intestinal obstruction. The usual site of stoppage is the terminal ileum. The condition is commoner than is generally supposed and should be thought of especially in elderly women who have had no previous abdominal operation. Roentgen examination may reveal air in the biliary tree, a visible gallstone, or signs of intestinal obstruction.

If a faceted calculus is found obstructing the intestine, a matching stone should be sought in the gallbladder. If one is found, cholecystostomy and removal of the calculus is indicated. Otherwise, it should be sought in the proximal small bowel. An interval cholecystectomy is recommended in cases in which symptoms from the diseased gallbladder continue, unless the patient is a poor surgical risk.

Six roentgenograms; 1 table.

PAUL MASSIK, M.D.  
Quincy, Mass.

**Intestinal Obstruction in the Newborn Associated with Faulty Development of the Midgut and Its Mesentery. A Description of Three Cases.** R. Spencer. *Surg., Gynec. & Obst.* 95: 568-578, November 1952.

The author presents 3 cases of acute intestinal obstruction in newborn infants. These are grouped together since they had a common feature, namely, inadequate fixation of the midgut and its mesentery to the posterior abdominal wall. This particular condition originates in malposition and non-rotation of the abdominal viscera, predisposing to volvulus. There are two forms of intestinal obstruction produced by this mechanism: constriction of the third portion



of the duodenum by the root of the mesentery and the partially closed loop obstruction of the volvulus itself. Frequently associated congenital anomalies are adventitious peritoneal bands and reflections and atresia or stenosis of the gut.

The author's 3 cases presented the clinical picture of intestinal obstruction, with vomiting as the predominant symptom.

Roentgenographic studies are the most important aid in diagnosis and of great value in locating the point of obstruction. The gas-distended stomach and duodenum may be demonstrated on a plain film. Absence of gas in the intestine below the duodenum is strong evidence of a complete duodenal obstruction. With partial obstruction, the intestine may contain gas shadows. A fluid level indicates a dilated loop containing fluid as well as gas. It is important that roentgenograms be obtained with the patient held erect, as well as in the prone position. A meal of barium diluted with milk may be given to confirm the findings on the plain film, but this procedure is not without danger.

Eight roentgenograms; 3 drawings.

ADAM PITOL, M.D.  
University of Pennsylvania

**Melanin Spots of the Lips, Oral Mucosa and Digits Associated with Intestinal Polyposis. Report of a Case.** Lloyd F. Sherman and Robert J. Tenner. *Minnesota Med.* 35: 1131-1134, December 1952.

The syndrome of melanin pigmentation of the lips, oral mucosa and digits associated with intestinal polyposis is described and the literature is reviewed. The pigmentation is most striking on the lips and buccal mucosa and varies from brown to almost black in color. It should not be confused with ordinary freckles. The other phase, intestinal polyposis, is most striking in the small intestine, particularly in the jejunum, although polyps have been present in the stomach, colon, and rectum. Polyps have also been reported in the nasal cavity and bladder in 2 instances. The condition appears to be hereditary, probably a simple mendelian dominant, which occasionally skips some generations.

This syndrome appears to be an entity distinct from the common colonic polyposis. When pigmentation of the type described is present, a diligent search for polyps is indicated, and follow-up studies are imperative because of the tendency to malignant change and the development of new polyps.

A case is reported, probably sporadic.

Two photographs. PAUL R. NOBLE, M.D.  
Pittsburgh, Penna.

**A New Technique for the Diagnosis of Carcinoma Metastatic to the Liver. A Preliminary Report.** Lloyd A. Stirrett, Eric T. Yuhl, and Raymond L. Libby. *Surg., Gynec. & Obst.* 96: 210-214, February 1953.

A new technic is described for the diagnosis of metastatic carcinoma of the liver, involving the use of radioactive iodinated human serum albumin ( $I^{131}$ HSA) as the tracer material and the scintillation counter as the detector of the gamma radiation from the  $I^{131}$ . [This procedure is described in a subsequent paper by the same authors in *RADIOLOGY* (The Hepatic Radioactivity Survey, *Radiology* 61: 930, 1953), and the details need not be repeated.] The accuracy of 96 per cent obtained in the series of 56 cases was main-

tained in the larger series (210 cases) reported in the later communication.

Two photographs; 3 drawings.

STEPHEN WARTELLA, JR., M.D.  
University of Pennsylvania

**Studies on Intrahepatic Arterial Circulation.** Frank Glauser. *Surgery* 33: 333-341, March 1953.

The arterial pattern of the human liver was studied following injection of a radiopaque material, a suspension of cinnabar (mercuric sulfide), into the hepatic arteries and small hilar vessels of fresh specimens obtained at autopsy. The author's conclusions regarding the hepatic circulation are as follows: (1) The branches of the hepatic arteries enter the liver substance along with, and under cover of, the capsule of Glisson. (2) There is no intrahepatic communication between the right and left hepatic arteries. (3) The right lobe of the liver is composed of secondary lobules each supplied by its own end-artery. (4) There are no arterial anastomoses between the smaller arteries of the liver. The vessels are all end-arteries. (5) There is a definite avascular plane between the right and the left lobe. (6) The rich intrahepatic anastomoses between the right and left hepatic arteries previously reported do not exist. They are all extrahepatic and are in the gastrohepatic omentum.

Seven roentgenograms; 1 photograph.

## HERNIA

**Diagnosis and Management of Esophageal Hiatus Hernia.** Joseph Shaiken. *Dis. of Chest* 23: 320-326, March 1953.

Ninety-five per cent of diaphragmatic hernias in the adult are said to occur through the esophageal hiatus. The incidence of this type of hernia has become known through fluoroscopic and roentgenographic examinations. These procedures not only determine the type, but the size of the herniated organ, the length of the esophagus, complications, etc.

Symptoms may be referred to the intestinal tract, to the heart, or to both. They include epigastric pain or discomfort related to meals, which may be relieved by vomiting, eructation of gas, alkalis, small meals, or eating in the erect position; acute or chronic blood loss (hematemesis or melena); substernal distress with pain radiating to the left shoulder and down the arm to the little or ring finger. Dyspnea, palpitation, cyanosis, and a sense of tightness in the chest may be due to actual displacement of the heart by the hernia.

Hernias may be constant or inconstant. The sliding or inconstant hernias may be more readily recognized by roentgen examination in the Trendelenburg position, with the Valsalva maneuver. Examination in the erect position will show whether the hernia returns to the abdominal cavity. Occasionally, a hernia can be recognized on the conventional postero-anterior film of the chest. A shadow behind the heart or a gas bubble above the diaphragm may be seen. Esophagoscopy is indicated to determine the presence of a mucous membrane erosion or ulcer in cases of bleeding.

Treatment is in general medical. Phrenicectomy, or surgical repair, is reserved for large hernias, or when medical measures fail.

Case histories are included, with 6 roentgenograms.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

**Right-Sided Traumatic Diaphragmatic Hernia Simulating a Pleural Effusion.** S. M. Unger. *J.A.M.A.* 151: 734-736, Feb. 28, 1953.

Right-sided diaphragmatic herniation of traumatic etiology is relatively uncommon. Of 432 previously reported diaphragmatic hernias, treated surgically, only 6 of the traumatic cases occurred on the right side.

The author's patient, a sixty-two-year-old white male, complained of a productive cough, vague upper abdominal pain that was more marked on coughing or deep inspiration, and dyspnea aggravated by deep inspiration. Later, chills and fever developed and the patient was admitted to a hospital. Roentgenography disclosed almost complete opacity of the right chest, and a diagnosis of pleural effusion was made. Thoracentesis yielded about a syringe of foul-smelling bloody fluid. The patient was treated for a lung abscess but failed to respond favorably. Constant upper abdominal pain developed and vomiting occurred with an increase in the pain. At this point the patient was transferred to a Veterans Administration Hospital, and again almost complete opacity of the right chest was demonstrated. Several irregular faint radiolucent areas with fluid levels were noted. Additional studies revealed numerous dilated loops of intestine with fluid levels in the right hemithorax. A barium enema examination showed the hepatic flexure of the colon entering the chest. At this time it was learned that the patient, twenty-three years previously, had been hospitalized for a broken back.

The preoperative diagnosis was traumatic rupture of the right diaphragm, with intestinal obstruction. At operation the ascending colon, which had a long mesentery, the cecum, and numerous loops of small intestine were found in the pleural cavity. The hernia opening lay posteriorly and was approximately 6 cm. in diameter. It contained a constricted segment of both large and small intestine. Anterior to the opening a loop of small intestine was adherent to the thoracic surface of the diaphragm. Because of gangrene of part of the herniated small bowel, a small intestinal resection was done, removing the site of perforation along with approximately 6 feet of small bowel. Convalescence was rather stormy because of the development of an empyema in the region of the operative site. Periodic x-ray examinations showed gradual re-expansion of the right lung and the patient was discharged ninety-nine days after admission.

Four roentgenograms. ALFRED O. MILLER, M.D.  
Louisville, Ky.

#### THE MUSCULOSKELETAL SYSTEM

**Psoriatic Arthritis.** Eugene H. Sterne, Jr., and Benjamin Schneider. *Ann. Int. Med.* 38: 512-522, March 1953.

Six cases of psoriasis and associated chronic arthritis are presented. Four patients gave a history of psoriasis of long duration preceding arthritic symptoms by from two to six years. In each of these, roentgenograms showed a distinctive type of destructive arthritis involving the phalangeal joints, and the changes were limited to the hands and feet. Two cases presented similar histories and similar distinctive changes in the distal phalanges of the feet or hands, but, in addition, other joints were involved with typical atrophic arthritis.

The authors believe that the destructive lesions of the

fingers and toes, in either the pure or the complicated cases, while not diagnostic of psoriatic arthritis, differ from those ordinarily seen in rheumatoid arthritis of considerable duration. In their series, except for one case, none of the involved areas showed the generalized demineralization commonly seen in long-standing rheumatoid arthritis. The distal interphalangeal joint changes in all cases were distinctly unlike changes seen in rheumatoid arthritis.

These distinctive roentgen changes vary with the stage and extent of joint involvement. In early stages there is a joint effusion; later, narrowing and irregularity of the joint surfaces are present. Osteoporosis is often found early in the disease process, but as the disease progresses the bones show increased density, followed by erosion of the involved joint surfaces, producing a thorn-like appearance of the fingers or toes.

From a study of these 6 cases and similar cases in the literature, one would be inclined to accept psoriatic arthritis as a separate disease, unrelated to rheumatoid arthritis and resembling certain types of neurogenic arthritis or the arthritis sometimes seen in chronic connective-tissue diseases.

Six roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**An Experimental Study of the First Radiologic Manifestations of Osteoporosis.** Giorgio Fusi. *Radiol. clin.* 22: 123-129, March 1953. (In Italian)

The author decalcified whole and sliced normal lumbar vertebral bodies with nitric acid and correlated the radiographic appearances of these specimens with the calcium loss. The first radiographic changes were seen when 3 per cent of the initial calcium content had been lost.

A decalcified vertebra and an untreated vertebra from the same specimen (as a control) were then placed beneath the lumbar region of a living person of moderate size, in order to evaluate the effects of superimposed soft tissues on the determination of demineralization. In such tests, approximating conditions *in vivo*, a loss of 60 per cent of the original content of calcium had to be sustained before radiographic differences between the normal vertebra and the demineralized one were appreciable.

[These findings are in keeping with previous reports showing the large amounts of bone destruction that may be present in vertebral bodies before this is detectable by routine radiographic methods.—C. V. C.]

Seventeen roentgenograms.

CHRISTIAN V. CIMMINO, M.D.  
Fredericksburg, Va.

**Osteopathia Striata—Voorhoeve's Disease. Report of a Case Presenting the Features of Osteopathia Striata and Osteopetrosis.** R. L. Hurt. *J. Bone & Joint Surg.* 35-B: 89-96, February 1953.

A new case of osteopathia striata is described and the literature is reviewed. The main radiographic features were longitudinal striations in all the long bones, irregular fan-like striation in the ilium, and a considerable increase in the density of the skull and ribs. Scattered dense areas were also demonstrable in the vertebrae.

The author found it difficult to determine whether this case should be classified as osteopathia striata or

atypical osteopetrosis. It differed from Voorhoeve's original case in the skull and rib changes, which were typical of osteopetrosis. It is suggested that the increased density in these bones may be due to an exaggeration of the process causing the striations in the long bones, in which event this case may represent a link between osteopathia striata and osteopetrosis, both conditions being due to the same developmental abnormality. A relationship of osteopathia striata to osteopoikilosis has also been suggested, the assumption being that the striations in the former and the nodular areas of the latter are manifestations of the same abnormal process.

The diagnosis of all three of the conditions mentioned above rests upon the radiological findings. Among other conditions from which osteopathia striata must be differentiated are dyschondroplasia, Paget's disease, metastatic carcinoma, Leri's melorheostosis, fluorine poisoning, and the osseous lesions of syphilis.

Thirteen illustrations, including 11 roentgenograms.

**Reversible Metastatic Calcification Associated with Excessive Milk and Alkali Intake.** Paul Wermer, Marvin Kuschner, and Edgar A. Riley. *Am. J. Med.* 14: 108-115, January 1953.

The authors report a case of widespread metastatic calcification associated with peptic ulcer and the prolonged ingestion of milk and alkali. The patient, a 67-year-old male, was admitted to the hospital in 1949, complaining of abdominal pain and postprandial vomiting of several months duration. Since 1928 he had been hospitalized intermittently for pulmonary tuberculosis. In 1936 a diagnosis of duodenal ulcer was made. For the following twelve to thirteen years the patient drank two to three quarts of milk daily, supplemented by Sippy powders, antacids, and alkalis, and for eight or nine years his diet had consisted almost entirely of milk, with an occasional egg. During the eighteen months prior to admission he had observed the gradual development of slightly painful swellings on his back, right shoulder, and right wrist. For approximately two months he had noticed progressive weakness, weight loss, anorexia, and pruritus. Roentgen studies showed bilateral pulmonary tuberculosis, a duodenal ulcer, calcific masses attached to the inferior angles of both scapulae, and similar masses in the regions of the right subacromial bursa and the head of the right ulna. Phenolsulfonphthalein excretion was less than 5 per cent. Blood urea nitrogen varied between 58 and 61 mg. per cent; alkaline phosphatase between 3 and 5 Bodansky units. On several occasions the serum calcium ranged between 10.8 and 11.8 mg. per cent, and the serum phosphorus between 3 and 5 mg. per cent. Acid phosphatase was 1 King-Armstrong unit, the serum cholesterol 230 mg. per cent, and total serum proteins 7.2 gm. per cent, with an albumin-globulin ratio of 4.9/2.3. The Sulkowitch test was normal, and a quantitative analysis of urinary calcium revealed an excretion of 0.312 gm. in forty-eight hours.

Following the elimination of milk and absorbable alkalis from the diet, x-ray examination demonstrated a gradual resorption of the masses at the right wrist and shoulder and left scapula. Blood chemistry studies, however, showed no significant change. The patient died in renal insufficiency about a year after his admission to the hospital.

Five roentgenograms; 3 photomicrographs.

**Vitamin D Poisoning with Metastatic Calcification. Report of a Case and Review of the Mechanism of Intoxication.** Charles W. Wilson, William L. Wingfield, and Elam C. Toone, Jr. *Am. J. Med.* 14: 116-123, January 1953.

A case of vitamin D poisoning following prolonged use of Nion D (activated ergosterol) is reported. The patient, a 62-year-old male, had had rheumatoid arthritis of the spine and many peripheral joints for twenty years and had taken 200,000 i.u. of Nion D daily for four of every six weeks for seven years. During the seventh year evidences of renal impairment became evident. Blood chemistry studies showed an elevated urea nitrogen and hypercalcemia. Roentgen examination revealed a calcified mass around the proximal interphalangeal joint of the right index finger and at the distal interphalangeal joint of the left fifth finger, and a moderately dense, non-homogeneous calcified mass, measuring 9.0 cm. in its greatest diameter, in the region of the neck and greater trochanter of the right femur. The patient was placed on a low-calcium diet and was advised to abstain from use of medication containing vitamin D. Roentgenograms taken about a year after the discovery of the metastatic calcifications showed disappearance of the calcium deposits around the finger joints, but there was no apparent change in the mass in the right buttock. Since this mass was causing a traumatic sciatic neuritis it was therefore removed. Fluid aspirated from it had approximately the same calcium-phosphorus ratio as normal bone.

The mode of action and the mechanism of intoxication with vitamin D is discussed. The authors emphasize the potential dangers of administering large doses of vitamin D preparations.

Three roentgenograms; 1 photograph.

**Lumbosacral Transitional Vertebrae. A Clinical and Roentgenologic Study of 400 Cases of Low Back Pain.** E. Hasner, H. H. Jacobsen, M. Schalmitzek, and E. Snorrason. *Acta radiol.* 39: 225-230, March 1953.

A roentgenographic study made of 400 patients with a view to investigating the mobility of the lumbar spine revealed sacralization in 30 patients and lumbarization in 10. Roentgenograms were taken with the patients in the sitting position with the spine flexed forward and backward, as well as on maximal lateral bending. Changes in the mobility of the lumbar disks were frequently demonstrable in both sacralization and lumbarization. These changes, manifested by altered angulation on lateral bending, must be taken as evidence of disturbances of balance of the lumbar spine. Signs of disk degeneration were observed in 9 of the 10 cases of lumbarization but in only half of the cases of sacralization.

The patients ranged in age from twenty-three to sixty-five years. Two-thirds of those with sacralization were within the fourth and fifth decades. In 2 patients with sacralization and 3 with lumbarization, reflex changes and sensory disturbances were noted. These were interpreted as indicating prolapse of a lumbar disk, but the diagnosis was not verified.

In their discussion, the authors stress the fact that sacralization and lumbarization can be diagnosed only by roentgenography.

The clinical findings and past history are of limited significance.

Treatment must aim at stabilization of the spinal

column. It is either conservative (rest in bed or a supportive brace) or operative. In the present series of cases conservative therapy was employed with good results.

Two roentgenograms; 2 tables.

A. WILSON BROWN, M.D.  
Shreveport, La.

**Diagnostic Lumbar Disk Puncture. Clinical Review and Analysis of Sixty-Seven Cases.** L. Walk. Arch. Surg. 66: 232-243, February 1953.

The author reports a series of 67 cases in which lumbar disk puncture was carried out. The technic employed was a modification of that originally described by Lindblom (Acta radiol. 34: 321, 1950. Abst. in Radiology 57: 612, 1951). The series included 5 cases in which the disks were normal, 15 cases of ruptured disk with only slight deformity of the nucleus pulposus, 26 cases of degeneration, and 21 cases of rupture of a degenerated disk. The roentgenographic and myelographic changes in each group are described, but the author is concerned chiefly with an analysis of the clinical findings. This leads him to the following conclusions:

"Pain on coughing is more frequent in disk rupture than in degenerated disks without rupture, whereas numbness is less frequent. A strongly positive Lasègue sign occurs oftener in disks with than without rupture; in simple rupture this sign usually disappears in some months, whereas in degenerated disks a strongly positive sign may be found in cases of various duration. Differences are even found in some of the other clinical symptoms and signs. As a working hypothesis, it seems justifiable to consider that two different clinical syndromes may be caused by the intervertebral disk—that of nerve root compression and that of irritation by a perineural spread of the contents of the nucleus pulposus. In many cases, there is a combination of the two.

"Disk prolapse, as diagnosed by myelography and by clinical findings, is not a homogeneous group if examined by disk puncture. In most cases there is a ruptured disk. However, in rupture with spread of the contrast medium there is an indication for surgery only if tissue sequestra are found in the spreading medium, or if there is a bulging of the edges of the rupture. If these conditions are absent, negative findings on operation are to be expected, even if there has been radiating pain on puncture; in these cases treatment should be conservative. In verified disk prolapse, puncture may demonstrate a degenerated disk but no rupture; those are the degenerated disks with local posterior bulging (concealed disks)."

Sixteen roentgenograms; 7 tables.

**Principles of Vertebral Tomography.** Ingemar Bokström. Acta radiol., Supplement 103, 1953.

Following a brief historical review of body-section radiography, the author discusses the principles of tomography and reviews the literature, setting forth the advantages and disadvantages of different technical solutions and tomographic apparatuses. The apparatus used in the present study, called the Danatome, is described in detail. It is a unidirectional type of tomography with 17° and 35° amplitudes. Theoretical and technical considerations of tomography are dealt with in some detail. These include the effective thickness of the investigated layer, the various factors in-

involved in reducing and increasing the depth of focus, the material thickness of the film and intensifying screens, and secondary radiation.

For tomography of the spine the author uses a 35° amplitude. For clinical cases 1-cm. intervals are used as a rule, and for regions of special interest 0.5-cm. intervals. The usual exposure time is 1.4 seconds for examination of the cervical and dorsal spine and for anteroposterior views of the lumbar spine. The kilovoltage in these cases varies between 60 and 75 at 50 ma.

Two effects of making many exposures are discussed. The first is the real danger of overheating the target. The heat storage capacity of the anode and its cooling curve should be considered in determining the proper interval between successive exposures. The radiation dose is the second effect which must be considered. The author finds that the radiation dose in obtaining anteroposterior views of the dorsal and lumbar spine as well as the lateral view of the dorsal is approximately 3 r (skin dose) per exposure. For the lateral view of the lumbar spine the skin dose per exposure is 8 r. These measurements are recorded with the inherent tube filtration of 1 mm. Al. They are reduced by about 45 per cent when an additional filter of 1 mm. Al is used, and by about 60 per cent with an additional filter of 2 mm. Al. "The relatively large radiation dose in tomography of the spine is a factor that to some extent makes it necessary to limit the indications for its use."

The main part of this paper is a report of an experimental and clinical investigation of the vertebral bodies in adults. The author notes that the object is "...to assess the value of the tomographic procedure compared with that of the standard method, in examination of the spine, in the hope of contributing to the solution of the question whether there are absolute criteria for the application of tomography. The question to be answered is whether, on the whole, there exist conditions in which the tomographic method may provide information that cannot be obtained by means of the standard examination carried out according to the established rules."

The experimental investigations were carried out on adult unmacrated postmortem vertebrae, normal and diseased. In some cases the specimen was placed in water barely deep enough to cover it and in other experiments the specimens were immersed in varying depths to secure both favorable conditions and conditions simulating those existing at clinical examination with respect to the object-film distance and secondary radiation. Selected clinical cases are described to illustrate the experimentally obtained results in all studies. After studying the normal architecture, the author studied artificially produced defects simulating fractures and osteolytic and osteoplastic lesions. The studies are well controlled and reported in detail. For the purposes of this abstract, only the final conclusions are noted.

The structure of the vertebral body can be studied in greater detail by the standard method than by tomography. This is due to intensification of the trabecular pattern in the direction of the movement of the tube and film and suppression of the others.

For visualization of the upper and lower surfaces, the longitudinal movement of the tube and film is most suitable. For the curved surface of the vertebral body the movement perpendicular to the long axis of the vertebra is preferable.



In demonstrating very small lesions of the upper and lower surfaces, tomography is absolutely superior to the routine technic. In cases of fractures and compression, tomography provides additional valuable information as to the localization and degree of severity of the lesion. In the diagnosis of small diffuse destructive lesions in the spongiosa, tomography has no advantage over the standard method.

Tomography is superior to standard radiography in demonstrating relatively large spongel defects. Studying water-filled spherical defects, 8 mm., 15 mm., and 20 mm. in diameter, with the specimen immersed in 6 cm. of water, it was found that the routine film showed the 20-mm. defect only, and that faintly, whereas the tomogram showed up both the 20-mm. and the 15-mm. defects clearly and the 8-mm. defect partially. Eight millimeters is approximately the lower limit of the possibility of demonstrating a water-filled defect by tomography. When the specimen was immersed deeper in water, thus increasing secondary radiation, the tomogram failed to show up the 8-mm. defect.

Movement of the tube and film perpendicular to the long axis of the vertebrae is superior to the longitudinal movement under conditions that permit visualization of the structure elements. Under clinical conditions, when the structure elements are barely visible or not visible at all in the tomogram, there is practically no difference in this respect between tomograms taken with the two different movements.

The smaller the diameter of transirradiated bone superimposed over the defect, the more readily can the latter be demonstrated. The content of the defect is of great importance. When the defects in the vertebral bodies were filled with paraffin, the routine films showed up the 15- and 20-mm. defects. Tomography was superior to the standard method in that the tomogram demonstrated also the 8-mm. defect, even under conditions resembling those in the living subject.

In senile osteoporosis the visibility of defects is reduced. This is due to smaller difference between the density of the bony substance and the bony defects. With standard radiographic methods, the lateral view is superior to the anteroposterior view in the demonstration of osseous defects. Tomography is markedly superior to the routine procedure in demonstrating the defects in the anteroposterior view.

In the clinical application of tomography, sections made at 1-cm. or 0.5-cm. intervals are justified. Defects that are large enough to be detected may then be demonstrated. The best tomograms of a spherical defect are obtained when the cuts are made at the level of and about the equator. Sections at the level of the "poles" may also demonstrate the lesion, though inadequately. Intensifying screens permit better visualization of the defect.

Increasing the pivot axis-film distance results in less satisfactory tomographic demonstration of the defect. In the experimental studies, the best results were obtained when the specimens were placed on the table top.

In some of the described clinical cases, tomography showed up areas of destruction that were not visible or were indistinctly seen on routine films. In these cases the absolute superiority of tomography was verified. In the majority of cases routine examinations disclosed the presence of the lesions but their extension and localization were more distinctly revealed by the tomographic studies.

Osteoplastic lesions were much more readily demonstrated by radiography than were destructive lesions of corresponding size. In experimental investigations, tomography was superior to standard studies in visualizing areas of increased density. In all the described clinical cases of osteoplastic secondary deposits, however, the changes were of such degree of density that areas of opacity were demonstrated both on the routine films and in the tomograms. Thus, although tomography sometimes shows up the osteoplastic lesions more clearly, its use in these cases is not justified.

"The technique of tomography has a useful place as a complement to the routine method in radiographic examination of the spine in selected cases, especially in those of small lesions in the upper and lower surfaces of the vertebral body and of relatively large destructive changes in the spongiosa, when a correct diagnosis is urgently required, because of its absolute superiority over the standard investigation.

"The use of tomography is also justified in selected cases to give a free projection of the spine by elimination of disturbing superimposed structures, such as skeletal parts, pulmonary structures and intestinal gas. For practical purposes tomography may be of great value in the examination of the regions that are difficult to radiograph, the upper cervical spine in the anteroposterior view, and the region comprising the lower cervical and the upper dorsal spine in the lateral view."

Sixty-seven illustrations, including numerous groups of roentgenograms.

BERTRAM LEVIN, M.D.  
Chicago, Ill.

**A Qualitative Comparison Between the Standard Type of Examination and Tomography for Certain Intraosseous Structural Changes.** Mackenzie Davidson Memorial Lecture. Folke Knutsson. *Brit. J. Radiol.* 26: 113-121, March 1953.

Conventional roentgenograms and tomograms were obtained of dried specimens of the spine and knee, both in air and immersed in water. Immersion in water was designed to introduce certain factors which are responsible for lack of definition in clinical practice, conditioned by focus-object-film distance and secondary radiation.

The first studies had to do with the structure of the cancellous bone of the vertebrae. Under conditions corresponding to those prevailing in the examination of a patient, the lack of definition in the tomogram was of such a high degree that the details of structure were appreciably blurred or completely obliterated, leading to the conclusion that for clinical studies of the structural pattern of the vertebral body the standard roentgenogram is to be preferred. Only in the case of extensive destruction of the trabeculae was tomography considered superior.

Studies were also made of specimens of the spine containing spherical defects of different size (8, 15, and 20 mm. diameter). For the demonstration of central defects in the cancellous bone tomography proved definitely superior to conventional radiography. By neither method was the smallest defect demonstrable when the specimen was immersed in water to simulate clinical conditions.

Discussing the clinical importance of tomography claimed by some authorities, the authors conclude that the ability of the procedure to reveal changes not apparent on the standard film is so inconsiderable as not to justify its use as a routine. Only in those cases where the diagnosis must be pressed to the utmost should its

absolute superiority, based on purely physical grounds, indicate the addition of tomography to the standard examination. For practical reasons, however, the use of tomography in examination of the vertebrae may be advisable. It often leads, by both simpler and surer means, to a satisfactory result.

Both clinical and postmortem material was used for the knee studies. These investigations proved the absolute superiority of tomography over the standard method in the demonstration of small bone lesions, and in the detailed analysis of the character and extent of a compression fracture.

Twenty-four groups of roentgenograms; 1 photograph of the tomographic apparatus.

[The author's material is drawn from basic research studies being carried out in his department in the University Hospital, Upsala, Sweden, by Fagerberg and Bokström. See the preceding abstract.—Ed.]

SYDNEY J. HAWLEY, M.D.  
Seattle, Wash.

**Diskography.** Raymond De Haene. *J. belge de radiol.* 36: 131-164, 1953. (In French)

Diskography adds two improvements to other means of studying disk lesions: it furnishes a direct image of the disk structure and it provides opportunity to reproduce the pain complained of by the patient, when the offending disk is injected.

Premedication includes barbiturates and opiates. The external needle is introduced into the spinal canal slightly off the mid-line opposite the side of pain. The internal needle is introduced into the disk through the lumen of the external needle. The contrast agent is 35 per cent Diodone (similar to Diodrast). Lindblom adds 0.5 c.c. of 5 per cent novocaine to each 2 c.c. of Diodone, and while some authors maintain that the addition of an anesthetic is not necessary, it is felt that this is justified by the occasional irritation of nerve roots or the meninges.

Injection of contrast agent should be performed only after roentgenograms show the needle to be in proper position. The healthy disk will receive about 0.5 c.c. of the medium. If the injected disk is responsible for the patient's symptoms, his pain will be reproduced.

If the perinuclear space is injected, two parallel plate-like bands of contrast material are seen on the roentgenogram. Injection of the disk proper yields a single oval shadow. The degenerated disk receives 2.0-2.5 c.c. of contrast medium and shows irregular projecting shadows.

Diskography is indicated in those patients in whom surgery is contemplated and in whom there is reasonable doubt (following clinical, roentgenographic, and myelographic studies) of the exact location of disk pathology. No serious reactions to the procedure were encountered in the author's series, which included more than 100 opacified disks. Others have reported such complications as infection of the disk, headache, abdominal and lumbar pain. Properly performed, the procedure involves little risk.

Twenty-seven roentgenograms.

CHARLES M. NICE, M.D.  
University of Minnesota

**The Diagnosis of Shoulder Lesions Due to Injuries of the Rotator Cuff.** V. H. Ellis. *J. Bone & Joint Surg.* 35-B: 72-74, February 1953.

The author refers briefly to Codman's criteria for

diagnosing an injury to the rotator cuff of the shoulder. His own paper is devoted to two diagnostic procedures. The first of these is procaine injection in the area of maximum tenderness followed by re-examination of the patient clinically. If, following the injection, abduction of 150 degrees or more is possible, it is considered that there is no major lesion in the rotator cuff. Otherwise the second procedure, arthrography, is indicated.

Of 14 patients in whom the range of abduction exceeded 150 degrees following procaine injection, 12 recovered completely. One of the 2 others was found on operative exploration to have a recent extension of an old minimal tear. Of the 11 patients who did not respond with increased motion, 7 showed a large tear at operation or did not recover. There were 3 equivocal cases, with recovery in 2. As a result of these observations, it is concluded that procaine injection, though not offering a completely accurate indication for treatment, may in some instances save unnecessary exploration of the shoulder joint.

Arthrography was employed in 42 suspected major tears and was found to be highly reliable whether the results were positive or negative. In 14 of 15 cases operated upon, the radiographic findings were confirmed. Of 20 patients with negative arthrograms, 15 recovered completely. The technic is described.

Two roentgenograms; 2 tables.

JOHN OLSON, M.D.  
Indiana University

**Epiphyseal Injuries of the Radial Head and Neck.** Sawnie R. Gaston, Frederick M. Smith, and Orren D. Baab. *Am. J. Surg.* 85: 266-274, March 1953.

The authors report a series of 74 cases of injury to the proximal radial epiphysis, presenting them in 4 groups, according to their pathological classification.

**Group I:** 24 cases diagnosed on clinical grounds alone. The children of this group complained of elbow pain, tenderness at the upper radial epiphysis, limited motion, and hemarthrosis of the elbow joint. Despite negative x-ray findings they were considered to have injured the radial epiphysis. Treatment consisted of a protective sling or splint. All recovered fully.

**Group II:** 39 cases with x-ray evidence of a fracture of the radial head and neck but with minimal or no displacement. The most frequent radiologic finding was a tilt of the radial epiphysis up to 15 degrees. Full function was regained without reduction.

**Group III:** 6 cases with fractures of the proximal radius with a tilt of the epiphysis of 20 to 70 degrees. Three patients, eight, nine, and eleven years of age, had no reduction and showed limitation of elbow motion up to three years following injury. X-ray examination showed enlargement of the radial head, premature closure of the epiphysis, but normal radial length. In the other 3 cases, in children of eight, twelve, and thirteen years, excellent reduction was obtained, and a three-and-a-half-year follow-up showed normal anatomy, full function, and slight widening of the radial neck on x-ray examination. Closed reduction is advisable in this group.

**Group IV:** 7 cases with fractures of the radial epiphysis associated with dislocation at the elbow. In all these cases there was complete avulsion with displacement and rotation of the epiphysis. The cases in this group are described in detail and the results analyzed. Open reduction is generally required for these patients.

In all instances of replacement of the radial epiphysis, it survived, and none of the patients showed a disturbance in radial length. Excision of the epiphysis may be done if necessary in girls of twelve years and boys of fourteen years or older. There follows a compensatory retardation of growth in the length of the ulna.

Proximal radio-ulnar synostosis as a complication in this type of injury seems to result in a large degree from late operation and undue operative trauma. To prevent this complication, operation later than forty-eight hours after injury should be avoided.

Thirty-two roentgenograms.

SEYMOUR A. KAUFMAN, M.D.  
Boston, Mass.

**Fractures of the Calcaneum, with an Atlas Illustrating the Various Types of Fracture.** C. K. Warrick and A. E. Bremner. *J. Bone & Joint Surg.* 35-B: 33-45, February 1953.

Three hundred fractures of the calcaneum have been divided into two main groups. The authors in this article concern themselves only with the second group, consisting of 224 compression-shearing fractures.

When the calcaneum is fractured as the result of the compression force and shearing strain experienced when the heel strikes the ground in the course of a fall, the fracture will extend forward and laterally from a point on the medial side at some distance behind the sustentaculum tali. This primary fracture may extend in three ways: (1) It may traverse the posterior articular facet; (2) it may enter the sulcus calcanei medial to the facet and then pass toward the lateral side of the bone; (3) it may pass behind the posterior articular facet to the lateral side of the bone. There is thus a lateral fragment and a medial fragment.

If the primary fracture is not associated with a secondary compression fracture of the lateral fragment, the following variations of fracture may be recognized: (1) fracture of the posterior articular facet without displacement; (2) fracture of the posterior articular facet with lateral displacement of the main lateral fragment; (3) fracture with diminution of the salient angle but without involvement of the posterior articular facet.

The above injuries represent only a minority of the compression fractures, because the force which caused the primary fracture usually will be great enough to drive the lateral fragment with its articular surface against the under surface of the talus, producing a secondary compression fracture of the main lateral fragment. This secondary fracture causes a depression and rotation of that part of the articular surface which lies lateral to the primary fracture. Depending on whether the primary fracture runs across the posterior articular facet or enters the sulcus calcanei, one of the following fractures is produced: (1) fracture with depression of the lateral part of the posterior articular facet; (2) fracture with depression of the entire posterior articular facet. Each of these two fractures is met with in two types. In Type 1 the part of the articular facet which lies lateral to the primary fracture is depressed into the underlying bone. In Type 2 the depressed articular surface is continuous with the upper part of the main lateral fragment, which is split horizontally. The lateral wall of the bone is frequently comminuted in these fractures and this comminution may extend forward to involve the lateral part of the calcaneo-cuboid joint.

To demonstrate fractures of the calcaneum, the authors use three radiographic projections: lateral, axial, and Anthonson's oblique projection (with the dorsiflexed foot in the lateral position on the film and the ray directed to a point just below the medial malleolus, with an angulation of 25 degrees cranio-distally and 30 degrees dorsoventrally).

An atlas of reproductions is appended to the text.

Thirty-eight illustrations, including 25 roentgenograms.

BASIL DULIN, M.D.  
Indiana University

**Naviculo-Cuneiform Fusion in the Treatment of Flat Foot.** Ewen A. Jack. *J. Bone & Joint Surg.* 35-B: 75-82, February 1953.

Radiological examination shows three anatomical types of flat foot, all of which are due to one or more breaks of the longitudinal arch of the foot. The break may occur at the talo-navicular joint alone, giving rise to a so-called perpendicular talus deformity; it may occur at the naviculo-cuneiform joint, or there may be relaxation at both joints. Clinically the differential diagnosis of the three types is difficult, but the defect is easily detected on lateral weight-bearing radiographs of the foot.

The author gives a full description of the operative procedure. The indications for operation are, in general, restricted physical activity in the face of conservative treatment.

The series of cases reviewed here included 46 feet in 25 patients between the ages of eleven and fourteen. Eighty-two per cent had satisfactory results. Eighteen per cent were classed as unsatisfactory. In the majority of these, it was found on further scrutiny that the break was not confined to the naviculo-cuneiform joint. Failure of fusion occurred before it was realized that early weight bearing must not be allowed.

The author feels that with good selection of cases the operation affords an excellent means of restoring a normal arch and preserving an almost fully mobile foot.

Seventeen illustrations, including 9 roentgenograms.

J. S. WHITMORE, M.D.  
Indiana University

## THE SPINAL CORD

**The Myelographic Appearance of Adhesive Spinal Arachnoiditis.** William B. Seaman, Sumner N. Marder, and Herbert E. Rosenbaum. *J. Neurosurg.* 10: 145-153, March 1953.

The myelographic appearance of 7 surgically proved cases of adhesive spinal arachnoiditis is presented. When obliteration of the subarachnoid space is total, a complete block is found on myelography. If obliteration is partial or patchy, filling defects or pockets are demonstrated. These appearances may be indistinguishable from the changes produced by either tumors or ruptured intervertebral disks.

Because of the occurrence of complete obstruction and filling defects, differentiation from intra- and extradural tumors is difficult. In the presence of a tumor, when a block is complete, the margin of the opaque column adjacent to the block is smooth. In the presence of arachnoiditis, it is ragged or irregular because of adhesions that extend beyond the point of the obstruction. This observation was made in 4 of the cases reported. However, in 4 patients, the presence of an

intraspinal tumor was suspected because of a large smooth filling defect.

In 3 cases, obliteration of a large area of the sub-arachnoid space was encountered and a diagnosis of arachnoiditis was considered likely, despite the absence of the "characteristic" myelographic picture.

Nine myelograms.

HOWARD L. STEINBACH, M.D.  
University of California

## GYNECOLOGY AND OBSTETRICS

**Relationships of the Female Urethra and Bladder in Urinary Stress Incontinence.** C. P. Hodgkinson. *Am. J. Obst. & Gynec.* 65: 560-573, March 1953.

The relationships of the urethra and bladder were investigated by means of a modified urethrocytographic technic in normal, asymptomatic patients and in patients with stress incontinence. The distortion caused by a semi-rigid catheter was eliminated by using a metallic bead chain which was inserted into the urethra and bladder by means of a longitudinally bisected soft No. 18 French catheter whose tip was altered to accommodate the chain. With the chain in place, the catheter was removed and, after emptying the bladder of urine with a glass catheter, 60 c.c. of 15 per cent Skiodan was instilled. Erect anteroposterior and lateral views of the bladder were taken with and without straining and the relationships of bladder, urethra, and symphysis were studied.

The urethrographic studies of the normal group showed the bladder floor to be at the mid-pubic level. The bladder was oval in shape. The floor was well supported and showed no downward thrust on straining. The internal urinary meatus was located near the junction of the posterior and middle thirds on the lateral films. After parturition, when there was no apparent loss of support, the bladder was elongated posteriorly and the internal urinary meatus was located at the mid-bladder plane. The urethra extended obliquely forward in a straight line. Near the external urinary meatus it curved sharply downward. Straining caused slight descent but no major deformity of bladder contour.

Continent multiparas with various degrees of bladder floor relaxation showed backward and downward rotation of the bladder with relative elevation of the internal urinary meatus from the area of maximum hydrostatic pressure.

Patients with stress incontinence showed downward vertical thrust of the bladder and urethra without rotation. The internal urinary meatus in these patients plunged to the most dependent bladder level, where it was subject to the maximum hydrostatic pressure during the straining effort. Surgical corrections of stress incontinence were shown either to restore normal anatomy or remove the internal urinary meatus from the area of maximum hydrostatic pressure. The author concludes that three factors of importance in urinary continence of females are: (1) intact sphincter mechanism; (2) hydrostatic pressure; (3) mechanical effect produced by downward and backward rotation of the bladder on the fixed or well supported urethra.

Nine illustrative cases are reported. Except for these case reports the paper is much like that by Hodgkinson and Doub in *Radiology* 61: 335, 1953.

Eight illustrations.

WARREN A. NAFIS, M.D.  
Jefferson Medical College

**Radiographic Diagnosis of Placenta Praevia.** P. E. Hiebert and Doris A. Kubin. *J. Kansas M. Soc.* 54: 113-115, March 1953.

A soft-tissue radiographic method of determining the site of the placenta is described. Three projections are made without contrast medium, with the patient upright, with 40 inches anode-film distance, kilovoltage appropriate for the thickness of the patient, 200 ma., and the Bucky diaphragm. The bladder is emptied before examination. The first projection is anteroposterior, including the pubis, ischial tuberosities, the trochanters, and the major portion of the abdomen on a 14 × 17-inch film, time 1 second. A left lateral view of the pelvis on a 10 × 12-inch film shows the sacral promontory, symphysis pubis, sacrum, coccyx, ischial tuberosities, and fetal head, time 1 3/4 second. A left lateral fetus film, 14 × 17 inches, shows the entire uterine wall, 1 second time. Most of the lateral fetus films will show a normally implanted placenta, some times with physiological calcification. If the greater portion of the placenta is not above equator, low implantation is suspected and evidence of displacement of fetal parts is sought.

According to Ball and Golden (*Am. J. Roentgenol.* 49: 731, 1943. *Abst. in Radiology* 42: 101, 1944), in the last trimester the head will normally dip into the pelvic outlet, occupying a mid-coronal and mid-sagittal plane position, if the mother is upright. Deviation from this is highly suggestive of placenta praevia marginalis or partialis. Marginal placenta praevia will cause an increase in the distance of the presenting part from the sacral promontory and inner margin of the pubic symphysis to 2.5 cm. or more, demonstrable on the lateral film. Placenta praevia centralis displaces the head directly upward, and this diagnosis is likely with such displacement in the absence of disproportion or a distended bladder, if the placenta is not visualized elsewhere. Sometimes a soft-tissue shadow indenting the anterior wall of the gas-filled rectum is seen in placenta praevia.

The authors believe their method will establish the diagnosis of placenta praevia in a high percentage of cases but present no statistics.

Two roentgenograms.

GEORGE A. SHIPMAN, M.D.  
New Orleans, La.

**One Thousand Complete Pelvimetries: A Radiological and Obstetrical Analysis.** Colin Macdonald and Shirley Thomas. *M. J. Australia* 1: 357-361, March 14, 1953.

The authors reviewed 1,000 pelvimetric studies made in both public institutions and private practice, in Australia, with a view to establishing normal values and determining what views and measurements constitute an adequate examination. The entire investigation was looked upon as a minor research project, and for this reason a rather elaborate series of projections and measurements was employed. In addition to (1) a view of the inlet obtained with the inlet plane roughly parallel to the table, (2) an erect lateral view (preferably in the last month of pregnancy), and (3) the usual outlet measurements, the studies included the two diameters suggested by Allen (*Brit. J. Radiol.* 20: 164, 1947. *Abst. in Radiology* 50: 272, 1948), namely, the symphysis-biparietal diameter and the available posterior segment diameter.

In 586 cases it was possible to correlate the obstetrical



results with the pelvimetric measurements. The range of diameters permitting normal labor was found to be as follows:

<b>Inlet:</b>	
True conjugate.....	8.5-14.3 cm. (av. 11.4 cm.)
Transverse.....	11.7-15.4 cm. (av. 13.2 cm.)
Posterior segment.....	2.7- 6.9 cm. (av. 4.6 cm.)
Inclination of brim.....	38°-77° (av. 60°)
<b>Mid-pelvis:</b>	
Bispinous.....	7.9-12.6 cm. (av. 10.4 cm.)
Superior antero-posterior.....	10.3-15.3 cm. (av. 12.8 cm.)
Inferior antero-posterior.....	9.6-15.0 cm. (av. 11.8 cm.)
Posterior segment.....	2.1- 7.0 cm. (av. 4.6 cm.)
<b>Outlet:</b>	
Bituberous.....	8.7-14.7 cm. (av. 11.4 cm.)
Posterior segment.....	5.4-10.6 cm. (av. 7.8 cm.)
Subpubic angle.....	65°-104° (av. 83°)
Symphysis-biparietal distance.....	5.4- 9.7 cm. (av. 7.1 cm.)
Available posterior segment.....	3.4-11.6 cm. (av. 6.6 cm.)

Exact figures, however, serve only as guides, since a narrow measurement in one respect may be compensated elsewhere. Other factors also enter into the problem, as the curvature of the sacrum, whether the side walls converge or not, and the breadth of the sacro-sciatic notch.

The authors conclude that "a case can be made out for pelvimetry which measures all three planes in the antero-posterior and transverse diameters, the outlook in labor being affected by the capacity of the pelvis as a whole." They suggest that "this range of pelvimetry can be justified: (i) inlet: true conjugate diameter, transverse diameter, posterior segment; (ii) mid-pelvis: bispinous diameter, superior antero-posterior diameter, inferior antero-posterior diameter, posterior segment; (iii) outlet: bituberous diameter, posterior segment, subpubic angle."

Five tables,

PAUL MASSIK, M.D.  
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## THE GENITOURINARY SYSTEM

**The Pathology of Urinary Calculi: Radial Striation.** J. A. Carr. *Brit. J. Urol.* 25: 26-32, March 1953.

Many calculi differing widely in composition and origin are marked on their fractured surface by radial striation. The author investigated this feature in 500 urinary calculi received consecutively for analysis. General observations with the aid of the binocular dissecting and petrographic microscopes were followed by x-ray diffraction studies. Radial striation on the fractured surface or nodularity of the external surface, which is considered as indirect evidence of radial striation, was present in 212 calculi, or 42 per cent. It occurred only in areas composed of calcium oxalate monohydrate, uric acid, or calcium acid phosphate dihydrate. Concentric lamination was always present in the radially striated areas.

The x-ray diffraction studies showed the striations to be a consequence of the arrangement of the minute crystals which form the calculus; all the crystals tend to have a particular crystallographic direction radially placed in the calculus. In the case of calculi composed

of calcium oxalate monohydrate this direction is the *b* crystallographic axis; in the case of calculi composed of calcium acid phosphate dihydrate it is the *a* crystallographic axis.

Having determined that the radial striation is an expression of the orientation of the component crystals, the author formulated a theory of pathogenesis of striated calculi from information available in certain geological concretions—spherulites—known to have their crystals similarly oriented. It is believed that the adherent mucinous layer which is found on freshly recovered calculi provides the necessary framework in which undisturbed diffusion of ionic groups can occur. This results in further oriented growth of the calculus, with incorporation of the mucinous layer as its organic matrix.

It is suggested that a further understanding of the pathogenesis of urinary calculi may indicate a new approach to their prevention.

Four illustrations; 2 tables.

**X-Ray Absorption and Diffraction Studies on Experimental Vesical Calculi.** I. Hedenberg, B. Engfeldt, and A. Engström. *Brit. J. Urol.* 25: 33-37, March 1953.

Microradiographic and x-ray diffraction studies were carried out on experimental vesical calculi produced in rats by a diet deficient in vitamin A. In one type of calculus the mineral salts were found to be arranged in concentric layers separated by layers containing organic substances but little inorganic material. In others the mineral salts in the nucleus were arranged in strands. The x-ray diffraction pattern of the mineral salts was characteristic of hydroxylapatite. Similar observations were made on a few spontaneous calculi in man.

No attempt is made here at a comprehensive study of crystal structure and the distribution of the components of calculi of various types. The paper serves, however, to stress the possibility of producing experimental calculi of a type similar to spontaneous calculi and of applying biophysical methods for their analysis.

Nine microradiographs; 3 diffraction patterns.

**Distortion of Pyelogram by Extrarenal Lesion: Liver Abscess Distortion of Pyelogram.** T. M. Yates. *J. Urol.* 69: 309-314, February 1953.

Distortion of the pyelographic pattern may be due to either primary renal or extrarenal causes. Three cases of proved liver abscess are presented, which caused pyelographic changes simulating primary renal disease. All three patients had recurrent episodes of right upper quadrant pain, right costovertebral angle tenderness, fever, and pyelographic evidence of a pressure deformity of the right kidney. Operation led to a correct diagnosis, and the patients' subsequent courses were unremarkable. Postoperative pyelograms were normal.

Liver pressure on the right kidney does not seem possible if normal kidney mobility exists. It is probable that inflammatory adhesions between the kidney and liver must precede any effect of a liver mass on the renal structure. The operative findings in the author's cases tended to confirm this view.

One should be cognizant of the possibility of a liver effect on the kidney when examining patients com-

plaining of right upper abdominal pain accompanied by fever.

Five roentgenograms.

EDWARD E. TENNANT, M.D.  
Jacksonville, N. C.

**Extraperitoneal Pneumography.** Donald R. Smith, Howard L. Steinbach, Richards P. Lyon, and Paul B. Stratte. *J. Urol.* 66: 953-959, December 1952.

Retroperitoneal structures are poorly visualized and differentiated on the conventional roentgenogram because of their homogeneous densities. Thirty years ago Carelli (*Bull. et mém. Soc. med. d. hôp. de Paris* 45: 1409, 1921) first described the perirenal air insufflation technic for clear delineation of the kidneys and adrenals, but the employment of this method has not become widespread because of the significant number of deaths attributed to venous (pulmonary) gas embolism.

To overcome this danger a newer method is now being used, employing oxygen (Ruiz Rivas: *Am. J. Roentgenol.* 64: 723, 1950. *Abst. in Radiology* 57: 618, 1951). A needle is inserted either into the sacral canal or into the presacral-retrorectal zone and approximately 1,000 to 1,200 c.c. of oxygen is injected (15 c.c. per kilogram of body weight).

The authors have adopted the latter method in their series of nearly one hundred cases. Modifying the technic somewhat, they obtain better results with the patient lying on one side for one-half of the air insufflation and then on the other side for the remainder of the injection. If a unilateral examination is to be done, the patient remains in one decubitus position only.

Oxygen is felt to be the safest gas and is administered at a pressure of about 20 cm. of water.

Films are taken with the patient in the prone position with the head of the table elevated 15 degrees. Various views are employed. Stereoscopic anteroposterior and lateral films are routine. Tomography, too, is often quite helpful. Films taken as long as two to four hours after injection clearly delineate the retroperitoneal structures.

Venous air embolism being the only serious complication anticipated, it was felt wise to do preliminary studies on dogs. Retroperitoneal air insufflations of various volumes at various pressures were done. Pressures of from 15 to 20 cm. of water seemed ideal. Helium was also tried, but oxygen, being absorbed more quickly, was found to be preferable.

Death from venous air embolism is attributed to a blockage of outflow from the right ventricle. The signs of this catastrophe are a loud cardiac murmur, cyanosis, increased venous pressure, fall in blood pressure, rapid thready pulse, and syncope. Placing the patient immediately in the left lateral decubitus position will often avert disaster.

If the patient is carefully observed during the insufflation and a low gas pressure is used, extraperitoneal pneumography should prove to be both a safe and valuable procedure.

Three drawings; 10 roentgenograms.

DAVID J. STEPHENSON, M.D.  
University of Pennsylvania

**Aneurysm of Accessory Renal Artery.** Harold A. Chamberlin and Michael S. Hovenanian. *J. Urol.* 69: 362-365, March 1953.

Aneurysm of the renal artery is considered to be of

relatively rare occurrence, only 100 cases having been reported. In recent years, however, the diagnosis has been made more frequently because of specific radiographic changes. The authors present a single case.

A forty-year-old man was admitted to the hospital for a dull pain in the left upper quadrant. He had had no previous urinary symptoms. The only findings of note on physical examination were moderate tenderness without spasm in the left upper quadrant and multiple punctate, bluish-red spider nevi on the nose, cheek, chin, and lips. The skin lesions had first appeared following a severe middle ear infection at the age of eighteen. Laboratory findings were unremarkable with the exception of excretory urograms. These showed normal collecting structures bilaterally. Just in front of the lower pole of the left kidney, at the level of the second lumbar vertebrae, anterior to the renal pelvis, was a circular area of calcification 2 cm. in diameter. Laminagrams placed this shadow in the plane of the kidney pedicle and it was believed to represent an aneurysm of the renal artery. Operation was carried out on the seventh hospital day and a calcified structure was readily isolated. It consisted of a main afferent channel and several efferent branches having the consistency of blood vessels but found to be entirely independent of the main renal artery. The structure was removed and the histologic diagnosis was aneurysmal dilatation of a poorly formed artery with secondary degenerative changes and calcification. The removed vessels were obliterated and no blood was found to course through their lumina.

Aneurysms of the renal arteries when calcified usually form a ring-like shadow with a radiolucent center and a periphery which may or may not be entirely calcified. The normal renal artery enters the hilus at the center of the kidney. In the case reported, the calcific shadow occupied a lower position, due to the occurrence of the aneurysm in an accessory artery which entered the parenchyma at the lower pole.

Three roentgenograms; 2 photomicrographs; 1 drawing.

LAWRENCE R. JAMES, M.D.  
Boston, Mass.

## THE BLOOD VESSELS

**The Arteriovenous Anastomoses as Seen in the X-Ray Film.** E. Vogler. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 322-329, March 1953. (In German)

Anatomical investigations have demonstrated that arteriovenous anastomoses occur normally in numerous organs. They represent a direct communication between the arterial high-pressure and the venous low-pressure vessels proximal to the capillary system and permit some degree of regulation of the peripheral circulation. These anastomoses open up if an obstacle develops in the peripheral circulation, irrespective of whether the obstruction is due to changes in the vessel wall, obliteration, spasm, or some other factor. These anastomoses may occur in the precapillary system or higher up in medium-sized vessels, or even in the large arterial and venous trunks of the extremities. Since the introduction of serial angiography, they have been plainly demonstrated. The smaller ones, in the precapillary area, cannot be seen on the film with the naked eye but their presence is indicated by a premature filling of the venous system. The larger ones are plainly visible.

Using the double injection method of Sgalitzer, the author takes serial films in each of the three stages of filling of the vascular system. The first film is taken during arterial filling, the second during capillary filling, and the third during the venous phase. Sgalitzer has demonstrated that immediately following injection, the iodine compound acts as an irritant and produces a spasm of the capillaries and the precapillaries. Then, as the iodine-containing compounds are vasodilators, the spasm of the capillaries relaxes, and during that phase the second injection is made, clearly demonstrating the capillary bed. Thus the author has been able to demonstrate that during the first injection, when the spasm of the capillaries and precapillaries produces obstruction to the circulation, the arteriovenous anastomoses are dilated and in full operation. Later, during the second injection, when the capillaries are functioning properly, the anastomoses have contracted and are barely or not at all visible.

Under normal conditions, the arteriovenous anastomoses are hard to demonstrate. In pathological conditions, however, they can often be plainly shown. The larger ones are seen as a direct communication between the artery and the vein or as a broom-like ramification of small arteries surrounding a larger venous trunk. Whether the larger communications were originally small is difficult to ascertain, but this seems possible, since they are most frequently present in cases of chronic disturbances of the peripheral circulation and are often associated with many smaller ones. They are present for the most part in association with involvement of the capillaries or the precapillaries, as in endangiitis obliterans or in ulcers of the lower leg, but are rarely seen in slowly developing complete obstruction of larger vessels, as in arteriosclerosis. In cases of this type, collateral channels are preferred.

The arteriovenous anastomoses seem to be safety valves which regulate the circulation according to the needs of the capillary system. The author has been able to test the function of the anastomoses by means of vasodilatory substances such as Hydergin (Sandoz). At first, 20 c.c. of a Perabrodil preparation (the equivalent of Diodrast) is injected into the arteries for the visualization of the vessels in the thigh (first injection). Then, after the injection of 40 c.c. of the same preparation, the vessels of the lower leg are demonstrated (second injection). While these films are being developed, 2 c.c. of Hydergin diluted with 20 c.c. of normal saline solution are injected and ten minutes later a third injection of 40 c.c. of Perabrodil is given. Serial exposures are made and the various films are compared. If the capillaries and precapillaries are still able to function and to respond to the vasodilatory effect of the Hydergin, the anastomoses will disappear or become greatly diminished in size, inasmuch as their valvular action is no longer necessary. These examinations are particularly valuable in establishing the status of the circulation in cases of ulcer of the lower leg.

Nineteen roentgenograms.

WILLIAM A. MARSHALL, M.D.  
Chicago, Ill.

**Subclavian Vein Obstruction. Report of a Case Studied by Venography and Relieved by Surgery.** Orville Horwitz and Harry F. Zinsser, Jr. *J.A.M.A.* 151: 997-998, March 21, 1953.

Instances of venous obstruction caused by congenital

lesions manifesting themselves late in life are relatively rare. Such a case is reported.

The patient was a woman of 44 years, complaining of pain, cyanosis, and edema of the left arm. Routine procedures failed to disclose any evidence of tumor or cervical rib to explain these symptoms. Venograms showed marked narrowing of the subclavian vein at a point just lateral to its junction with the internal jugular vein. At operation, the subclavian vein was found to have a normal course anterior to the scalenus anticus muscle, which, however, was approximately twice its normal diameter. Although the vein lay between the enlarged muscle and an aberrant branch of the transverse cervical artery, no certain evidence of pressure was seen and no thrombosis was detected. The aberrant vessel and the scalenus muscle were sectioned at surgery and perivenous stripping of the subclavian vein was performed, followed by steady remission of signs and symptoms.

The cause of the obstruction is an interesting point for speculation. The authors favor the view that the obstruction was due to compression between the scalenus anticus and the anomalous artery, which disappeared with the relaxation incident to anesthesia.

One roentgenogram. LAURENCE R. JAMES, M.D.  
Boston, Mass.

**Technique of Abdominal Aortography.** Erik Lindgren. *Acta radiol.* 39: 205-218, March 1953.

The various technics of abdominal aortography are discussed, and a modification of the catheter method and a new apparatus for injection are described.

The author uses a size 240 or 200 polyethylene catheter with a 50-c.c. syringe filled with 40 c.c. of water-soluble contrast medium (70 per cent Diodrast, Umbradil, or Diodone). This is injected in a maximum of six to seven seconds through the catheter, which has been inserted into the femoral artery. Compressed air is used to obtain the 7 to 8 atmospheres of pressure necessary to make the injection within the time specified.

Eight roentgenograms; 4 photographs.

A. J. NICHOLAS, M.D.  
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**Recent Improvements in Translumbar Aortography.** A. Keller Doss. *J. Urol.* 68: 950-952, December 1952.

The author recommends the use of 70 per cent Urokon sodium (Mallinckrodt) for translumbar aortography. Injection of up to 30 c.c. of this medium in three or four seconds by means of a specially constructed 18-gauge needle with a 17-gauge bore was found to produce uniformly clear arterial delineation with less toxicity than 80 per cent sodium iodide.

Two roentgenograms; 1 photograph.

ADELE KYNETTE, M.D.  
University of Pennsylvania

**Translumbar Aortography in Infants Utilizing 70 Per Cent Urokon as a Contrast Medium.** W. F. Melick, T. D. Boler, and H. Black. *Missouri Med.* 50: 179-182, March 1953.

The authors present a brief general discussion of the merits of 70 per cent Urokon as a contrast medium in aortography and call attention to the lack of information on infant aortography. They present the history of a male infant first seen at the age of five and a half

weeks with bilateral hydronephrosis due to bladder neck contracture. A suprapubic cystotomy was done, and ten months later aortography was used to investigate the condition of the right kidney, both intravenous and retrograde pyelograms having been unsuccessful. The technic of the procedure is outlined.

The authors believe this is the first use of translumbar aortography in a patient so young. While they do not advocate the procedure in children as a routine, any more than in the adult, they do believe that in these young patients, where conservation of renal substance is of paramount importance, aortography may be of great usefulness. The availability of a non-necrotizing medium, Urokon sodium 70 per cent, has eliminated many of the dangers of the procedure.

Eight roentgenograms.

R. F. LEWIS, M.D.  
Cleveland Clinic

#### Translumbar Arteriography. A Survey of Its Uses.

Robert P. Schach. *South African M. J.* 27: 247-250, March 21, 1953.

The author first gives a concise, informative description of the technic of translumbar arteriography. The most widely accepted use of the procedure is in the differentiation between a renal tumor and a solitary renal cyst, when a soft-tissue mass has been seen on a plain film.

By demonstrating the renal blood supply one is able to learn something of the potential function of the kidneys. When surgery is contemplated for hydronephrosis, the knowledge of the blood supply to that kidney is a helpful point in determining whether nephrectomy or pyeloplasty is the operation indicated.

In deciding whether to do radical or conservative surgery in cases of staghorn calculi, multiple calculi, or a calculus obstructing the ureter, it is again advantageous to have information concerning the blood supply of the involved kidney.

Knowledge of the course of aberrant arteries is helpful prior to surgery. When operating on anomalous kidneys, it is good to know the number, location, and length of the arteries. Arteriography is useful, also, in diagnosing renal hypoplasia or agenesis. It has been used successfully in diagnosing renal infarction.

In hypertension, if the ischemic process is found to be unilateral, nephrectomy may be curative.

Occlusion or aneurysms of the aorta or any of its major abdominal branches can be demonstrated by arteriography. Tumors other than renal tumors are sometimes discovered. The site of implantation of the placenta has been successfully outlined.

The author offers this as a procedure not difficult to perform and of wide diagnostic application.

GEORGE A. SHIPMAN, M.D.  
New Orleans, La.

**Arteriography. A Simple Technique.** Ian MacKenzie and H. A. R. Hamilton. *Brit. J. Surg.* 40: 442-444, March 1953.

The authors describe a simple method of arteriography of the lower extremity. Light general anesthesia is preferred to either local or spinal anesthesia because of the assurance of complete immobilization. The extremity to be examined is positioned with the hip in full external rotation and partly abducted and flexed; the knee is flexed to a right angle or less. The cassette containing the film is so placed

as to include as much as possible of the thigh and the whole limb as far as the lower third. A portable x-ray apparatus has given good results.

Under surgical asepsis, the common femoral artery is exposed below the level of the inguinal ligament, and 20 c.c. of 70 per cent Diodone solution (Pyclosil 70) is injected through a No. 18 or 19 needle inserted proximally into the central portion of the vessel. The rate of injection is approximately 1.5 c.c. per second, with radiography after 15 or 16 c.c. have been injected. The film is then processed and inspected before closure of the incision, so that a repeat examination can be performed should the results not be satisfactory. The whole operation can, with practice, be completed in twenty minutes.

This method is considered to yield accurate information concerning the location and extent of blockage in vascular occlusion of the lower extremities, as well as the degree of collateral circulation in many cases; in others the obliterative process can be assessed only in general terms. No complications have been observed. Patients are ambulatory twenty-four hours after the procedure.

Four roentgenograms; 1 photograph.

J. L. CLEMENTS, JR., M.D.  
Atlanta, Ga.

**Temporary Block of a Branch of the Pulmonary Artery for Selective Angiography.** G. Tori and D. Petrucci. *Radiol. med. (Milan)* 38: 1171-1177, December 1952. (In Italian)

The authors employ transcatheter catheterization of the pulmonary arteries and, by manipulating the catheter, insert its tip in a vascular branch of their choice. The tip of the catheter is surrounded by a small rubber balloon the distention of which isolates the vascular territory to be studied. After the catheter is placed and the balloon distended, 5 to 8 c.c. of 7 per cent Pyclosil are injected in the vessel. The radiographs of selected branches of the pulmonary artery shown by the authors are beautiful, and the technic is quite intriguing, but one cannot help wondering about the practical application of such procedures.

Eight roentgenograms.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Ascending Erect Phlebography. Management of Chronic Venous Insufficiency of Lower Extremity.** E. M. Colvin, J. Frank Walker, and Horace D. Smith. *Arch. Surg.* 66: 292-300, March 1953.

The authors have used the technic of phlebography introduced by Scott and Roach of Johns Hopkins University (*Ann. Surg.* 134: 104, 1951. *Abst. in Radiology* 58: 909, 1952) in 75 patients. It consists of injecting 25 c.c. or more of 35 per cent iodopyracet (Diodrast) into a vein on the dorsum of the foot while the patient is in the upright position. A tourniquet above the ankle obstructs the superficial venous system. Roentgenograms of the leg are then taken.

The authors' patients, with few exceptions, represented definite problems in evaluation of deep venous circulation. In all of this group the information obtained was of value either on the basis of positive or of negative findings. In several instances the roentgenographic information differed from the impression gained by history and clinical examination.

Ascending phlebography with the patient erect is



felt to offer the most practicable and physiologic method for roentgen examination in chronic venous insufficiency of the lower extremity. It provides complete filling of the veins and reproduces normal anti-gravity mechanisms and hydrostatic pressures, aiding in the demonstration of valves and incompetent communicating veins between the superficial and deep

systems. This procedure is not indicated in the usual case of varicose veins but should be employed in patients with a history of deep thrombophlebitis or when there is doubt concerning the status of the deep venous system.

Seven roentgenograms.

PAUL MASSIK, M.D.  
Quincy, Mass.

## RADIOTHERAPY

**The Treatment of Cerebral Gliomas with 24-Million-Volt X Rays.** D. A. Layne, Valentine Logue, W. V. Mayneord, Wylie McKissock, and D. W. Smithers. *Lancet* 1: 516-519, March 14, 1953.

The authors give an account of the first clinical experiments to be carried out in Great Britain in the treatment of malignant tumors with a 24-mev electron-synchrotron. Following installation of the machine in the Royal Cancer Hospital in the summer of 1949, preliminary physical and biological studies led to the conclusion that such advantages as exist in the therapeutic effect of the x-rays produced at this high voltage arise rather from the superior distribution of absorbed energy in the tissues than from any fundamental difference in the nature of their biological actions.

A group of patients with cerebral gliomas was chosen for treatment for three reasons: (1) because it was desired to irradiate through bone to explore the advantage of lack of differential absorption obtainable with radiation of this quality; (2) because this group of patients had an unfavorable prognosis, but at the same time provided some prospect of a sufficient degree of localization of the disease to give the treatment a fair test; (3) because the limitations of the apparatus made necessary selection of a part of the body which could be placed accurately in the path of a horizontal beam of small size.

The plan of treatment was to attempt to give a tumor dose of 7,000 r in seven weeks to the smallest volume of tissue consistent with inclusion of the whole of the estimated extent of the tumor. The clinical trials began in May 1950 and the present report deals with 10 patients and the results attained in this small group up to December 1952. The series included 3 tumors diagnosed by ventriculography but not verified histologically and 7 astrocytomas (2 Grade I, 4 Grade II, 1 Grade III). At the date of the report, all but one of the patients was alive, having suffered little disability and no permanent epilation as a result of irradiation. The early response to treatment is said to have been better than has been observed before in similar cases, but, as the authors recognize, the period of observation is too short for any but preliminary conclusions.

Five illustrations; 1 table.

**Intrathoracic Irradiation of the Hilum After Resection for Bronchial Carcinoma. A Preliminary Report.** W. E. J. Schneidrzik. *J. Thoracic Surg.* 25: 327-328, March 1953.

A method of direct irradiation of the hilar structures following surgery for bronchial carcinoma has been developed. Immediately after the pneumonectomy or lobectomy has been performed, a Foley catheter (the bag of which should hold about 30 c.c. without tension) is introduced into the thoracic cavity through a stab wound. The bag is placed in such a position

as directly to overlie the hilus and is held in place by two chromic catgut sutures. A hole is then cut in the big catheter below the site of the bag, which ensures free drainage of fluid accumulating after the operation.

After the thorax has been closed in layers, the big catheter is connected to an underwater drainage and is treated like any ordinary drainage tube. This permits the introduction of radioactive cobalt into the Foley bag without soiling the thoracic cavity.

This method of treatment was employed in 2 cases, following pneumonectomy performed for bronchial carcinoma with hilar involvement. The irradiation was started on the eighth postoperative day by injecting 30 c.c. of liquid radioactive cobalt chloride into the Foley bag and leaving it there for six and one-half days. The radioactive fluid was then aspirated and the catheter removed. The patients had to be well isolated during the treatment, as radioactive rays could be traced with the Geiger counter in the adjoining room. The results are not given beyond a statement that the patients left the clinic "in a satisfactory condition."

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Observations on Radiotherapy of Bony Metastases of Breast Carcinoma.** K. Overhof. *Strahlentherapie* 90: 53-58, 1953. (In German)

The author reports 6 cases of solitary bony metastases of breast cancer which regressed entirely after x-ray therapy. Freedom from symptoms and bony restoration as shown roentgenographically had been maintained in some cases up to three years. Irradiation alone was successful, without administration of hormones. Hormonal treatment in addition to radiation may be beneficial; of itself it is insufficient.

Twelve roentgenograms. LEWIS L. HAAS, M.D.  
Chicago, Ill.

**Post-Irradiative Prophylactic Extraperitoneal Lymphadenectomy in Carcinoma of the Uterine Cervix.** Gunnar Gorton. *Acta radiol., Supplement* 100, 1953.

The author has done a very good job of reviewing the literature and compiling statistical data and charts on the incidence of lymph node involvement of the cervix and its treatment. He includes the results of both surgery and irradiation as reported by the top men in their fields from 1905 to 1948 and compares their findings with a series from the Konung Gustaf V's Jubileumsklinik, Lund, in which lymphadenectomy was performed or attempted following a prescribed program (Stockholm method) of irradiation. All stages and all age groups were included, which tends to give a true overall picture of the pathology and results of treatment.

In his summary, the author states succinctly the conclusions reached on the basis of his review of the literature: "that the five-year recovery rate for cases treated by irradiation only is about 40 per cent; that surgery is not superior to radiotherapy; that it is not possible to deliver an adequate dose to the lymph nodes along the pelvic wall; that the pelvic lymph nodes are common sites of recurrence; that carcinomatous involvement of the pelvic lymph nodes cannot with certainty be recognized before radiation treatment or operation; that carcinomatous involvement of the pelvic lymph nodes adds considerably to the distress of the patients in the later stages of the disease."

It was due to these findings that, in 1947, post-irradiation extraperitoneal lymphadenectomy was introduced as a routine procedure for Stages I and II, in the treatment of carcinoma of the uterine cervix at Konung Gustaf V's Jubileumsklinik. With this procedure, a small but steady increase in the survival rate has been obtained. Observations of the series of cases thus treated and the results obtained led to the conclusion that, until some method of delivering an effective dose of radiation to the lymph nodes along the pelvic wall is devised, "radiation treatment should be supplemented by extraperitoneal lymphadenectomy in Stages I and II, this procedure not only improving the recovery rate but also sparing the patient from metastases to the pelvic wall, a spread known to be accompanied by severe pain. As the treatment is a combination of irradiation and surgery, and as the one procedure must be adjusted to the other, as circumstances require in the individual case, it is recommended that both radiotherapy and surgery be placed in the hands of one and the same person."

This monograph includes an excellent description, with drawings, of the pelvic blood vessels and lymphatic systems, an outline of the Stockholm method—the standard and accepted routine radiation treatment of carcinoma of the uterine cervix at the Konung Gustaf V's Jubileumsklinik—and the details of the operative procedure of extraperitoneal lymphadenectomy.

Two hundred and twenty-nine case histories are appended, each with an accompanying drawing; 37 tables.

THOMAS E. PADGETT, M.D.  
University of Louisville

**Treatment of Cervical Stump Carcinoma.** Galen M. Tice. J. Kansas M. Soc. 54: 98-102, March 1953.

Of 240 cases of carcinoma of the cervix given their primary radiation therapy at the University of Kansas during the twenty-year period 1933 to 1953, there were 26 involving the cervical stump. Thirteen of these were diagnosed within twenty-four months after hysterectomy for other causes and were thought, therefore, not to be true stump carcinomas but carcinomas of the cervix which had probably been overlooked at surgery.

Radiologists must treat stump carcinoma regardless of how long after surgery it is discovered. Of the 26 patients treated by the authors, 12 were living at the time of the report and 14 were dead. The average duration of life after treatment in the fatal cases was two and one-half years, including 2 patients who were moribund when first seen. These two were treated palliatively to control bleeding. Seven of the 12 living have remained well for over five years (one over ten years); one is alive after eight years but with signs of cancer.

Early cases were treated with radium applicators in contact with the cervical stump, but close approximation was difficult and prolonged application occasionally injured the bladder or gut. Needles were also tried, but the best results have been obtained with transvaginal x-ray therapy, h.v.l. 1-1.5 mm. Cu, 500 to 750 r daily up to 5,000 to 10,000 r (7,000 r average). External irradiation through two anterior and posterior ports, delivering about 2,400 r to the mid parametria, is given at the same time. Additional lateral and perineal portals are used when they are felt to be necessary.

The author's five-year cure rate was 23 per cent, which is about the same as reported by others. Of the 12 living patients, 9 were treated transvaginally; of the 14 dead, only 4 were treated by the transvaginal technic.

Four tables.

GEORGE A. SHIPMAN, M.D.  
New Orleans, La.

**Combined Surgery and Irradiation in the Treatment of Cancer of the Cervical Stump.** Henry A. Young and August F. Jonas. Surg., Gynec. & Obst. 96: 288-294, March 1953.

The authors discuss the incidence, mode of lymphatic spread, clinical evaluation, and therapy of carcinoma in the retained cervical stump. The average incidence of this type of involvement in several series of carcinoma of the cervix was 4.1 per cent.

Lymphatic spread of carcinoma of the cervical stump follows a constant pattern within the pelvis before extending beyond it. Besides lymphatic spread there may be spread by continuity, contiguity, and by blood-vessel invasion. The authors believe that node involvement has about the same incidence in carcinoma of the stump as in carcinoma of the intact cervix. Distant metastases are fairly frequent.

Factors favoring surgery over radiation in selected Stage I and early Stage II cancers of the stump are: (1) prediction of radiation resistance by competent cytologists; (2) failure of radiation to deal more successfully with involved regional nodes; (3) local recurrence following apparently adequate irradiation; (4) technical difficulties and limitations of radium application to the cancer-bearing stump; (5) stenosis of the upper vagina as a result of previous external roentgen therapy, making radium application almost impossible; (6) greater incidence of post-irradiation complications in cancer of the cervical stump than in treatment of carcinoma of the cervix in the intact uterus; (7) the success of surgery in the hands of Bonney, Taussig, and Meigs.

Carcinoma *in situ* of the cervical stump should be treated by vaginal or abdominal cervicectomy. Stage I and Stage II radiation-resistant cases should be subjected to radical abdominal cervicectomy combined with the bilateral Taussig pelvic lymphadenectomy. Stage III and Stage IV radiation-resistant cases should be considered for pelvic evisceration, but this operation should be done only in institutions that are equipped for postoperative care of the patient. Stages I, II, and III radiation-sensitive cancers of the stump, after local control by irradiation, should be subjected to bilateral extraperitoneal lymph node dissection. This operation can be done by the average surgeon without undue risk.

In cases where it has been necessary to do a subtotal hysterectomy, the authors urge inspection of the re-

tained cervix every three months to detect any incipient inflammatory or neoplastic change.

One drawing.

JOHN J. CRAVEN, M.D.  
Cleveland Clinic

**Recurrences after Treatment of Malignant Tumors of the Female Genitalia.** H. Czech and R. K. Kepp. *Strahlentherapie* 90: 117-142, 1953. (In German)

A cancer is to be regarded as recurrent if it reappears after at least six months of complete absence of symptoms and proved disappearance of the primary tumor. In ovarian tumors this minimal interval should be one year. The results of operation and of irradiation for recurrences have in general been unsatisfactory. At the Gynecology Clinic in Göttingen a method of irradiation productive of better results has been developed. It involves high dosage, highly fractionated, combined with intravaginal irradiation. (Data as to dose and technic are not detailed.) Severe reactions occur more frequently and are of greater extent following the treatment of recurrences than after irradiation of the primary lesion. In spite of this, the results are at least as good as those of radical eviscerating surgery. The cure rates for recurrences reported by the authors are: cervical carcinoma, 18.5 per cent; corpus carcinoma, 29.2 per cent; vaginal carcinoma, 23.5 per cent; carcinoma of the vulva, 7.2 per cent; ovarian carcinoma, 18.7 per cent.

Six tables.

LEWIS L. HAAS, M.D.  
Chicago, Ill.

**The Place of External Irradiation in the Treatment of Osteogenic Sarcoma.** R. C. Tudway. *J. Bone & Joint Surg.* 35-B: 9-21, February 1953.

A total of 33 cases of osteogenic sarcoma, 8 osteolytic and osteoblastic, are considered in this paper. While the numbers are too small for statistical deductions, the detailed study of the cases provided useful pointers.

Histologically, it was found that the mitotic ratio (the ratio of the total number of tumor-cell nuclei counted to the number found to be in mitosis) was most valuable as a prognostic guide, showing a definite relationship to the grade of malignancy. The following ranges were found: Grade I tumors, mitotic ratio greater than 400 to 1; Grade II, between 400 to 1 and 100 to 1; Grade III, less than 100 to 1. Radiologically there is no clear-cut criterion by which to classify the cases. On the whole, the group with better prognosis shows a predominance of bone reaction over destruction, and the cortex is expanded or thickened rather than destroyed. Subperiosteal new bone formation is present, perhaps markedly so, but evidence of erosion of this new bone is absent or slight, and late in appearance, while sunray spicules are not marked. Codman's "triangle" is absent in these cases, and this is perhaps the only clear sign. Osteolytic sarcomata tend to arise centrally, showing a central area of destruction which involves the cortex without expanding it, and produces some periosteal reaction.

Of the 6 patients with Grade I tumors, 5 were still alive with no recurrence, 4 for five years or more. Of patients with an atypical clinical history suggestive of an inflammatory lesion, 4 survived, apparently free of disease, and 1 died after surviving six years.

The cases that did badly, whatever the treatment, were the following: (1) cases of Grade III histology;

(2) cases of Grade II histology with pre-existing bone disease; (3) cases in the older age group (over forty or fifty); (4) tumors located where adequate treatment was impossible; (5) most osteolytic tumors.

These factors are discussed, and illustrative case reports presented. On the basis of these findings, certain suggestions for treatment of these tumors are given.

"1. Deep x-ray therapy in high dosage, followed by local resection, should be given serious trial especially: (1) in the upper limb; (2) in the group with atypical clinical or radiographic signs, or histology resembling that of inflammatory lesions; (3) with Grade I histology; and (4) in the young.

"2. Deep x-ray therapy followed at once by amputation should be used for osteogenic sarcoma if: (1) local resection would leave a lower limb more unstable than an artificial leg, or (2) if response to x-rays is poor.

"3. Deep x-ray therapy alone should be used: (1) if the patient is unsuitable for, or refuses, any operation, and (2) palliatively if metastases are present or the tumor is too advanced or the patient is not fit for radical treatment.

"4. Amputation alone should be used palliatively, for pain or fungation, when x-ray therapy has failed to relieve, or is not readily obtainable."

The purpose of preoperative radiation is to render the tumor more quiescent and make dissemination less likely during the preoperative and operative stages.

Seven roentgenograms; 2 graphs; 2 tables.

H. GRIFFITH, M.D.  
Indiana University

**Radio-resistance and Development of Resistance of Malignant Tumors.** Gerhard Schubert. *Strahlentherapie* 90: 59-77, 1953. (In German)

The actual radiosensitivity of a tissue is the product of primary radiosensitivity and radioresistance. As a criterion of sensitivity, cell death is generally used. Sensitivity to radiation is based on the reaction of structural elements of the tissues: cell complexes, cells, and cell elements (genes). Sensitivity decreases with aging of the cells and with their degree of differentiation. It may also be influenced by physical, physicochemical, and chemical factors, such as temperature, water metabolism, blood supply, drugs, differences in irradiating agents, time factor, etc.

Normal cells and tumor cells differ in radiosensitivity. Upon this difference depends the radiosensitivity or radioresistance of the tumors.

Glücksmann held that when a biopsy of cervical carcinoma showed definite regression ten days after one radium application, the tumor was sensitive and the prognosis good; if no change were observed, the tumor remained resistant thereafter. The present writer and his associates could not confirm these observations. Among 61 cases they found an agreement between the first biopsy and final course in only 39.

Extension and mode of growth of cancer rather than histology are the determining factors in the results of treatment. The dose is not decisive, but higher doses secure a higher cure rate.

The causes of radioresistance and sensitivity are not clearly understood. Langendorff's target theory may give a useful explanation: the number, size, and sequence of ion-hits on the structural cell elements determine the degree of radiosensitivity.

Increasing resistance after repeated radiation may be explained by (1) slow adaptation (artificially produced mutation), or (2) spontaneous mutation. The author assumes that the increased radioresistance develops via spontaneous modification of mutations of cell elements.

Eight photomicrographs. LEWIS L. HAAS, M.D.  
Chicago, Ill.

**Radiotherapy of Benign Uterine Bleeding.** Hans-Joachim Fiebelkorn. *Strahlentherapie* 90:25-33, 1953. (In German)

In the treatment of simple climacteric metropathies radiotherapy has entirely replaced hysterectomy. For myomata, however, the use of radiotherapy is

limited. Fast growth, compression symptoms, submucous and subserous localization, pregnancy, early age, giant size, and uncertain diagnosis require surgery.

An ovarian dose of 290 r x-rays usually produces amenorrhea and avoids unpleasant climacteric complaints; however, 400 r is preferred. For bleeding due to myoma the author advocates intrauterine radium application. This is equivalent in effect to roentgen therapy, except for large nodes, for which x-rays are superior. In climacteric bleeding, intracavitary radium treatment with weak filtration is recommended. Prior to irradiation, the diagnosis must be confirmed histologically.

One graph; 4 tables. LEWIS L. HAAS, M.D.  
Chicago, Ill.

## RADIOISOTOPES

**The Treatment of Hyperthyroidism with Radioactive Iodine,  $I^{131}$ .** Max S. Allen, H. H. Dunham, Charles E. Montgomery, and Eugene T. Siler. *J. Kansas M. Soc.* 54:120-123, March 1953.

The authors have treated 121 thyroid cases with  $I^{131}$  at Kansas University since May 1950. Of these, 9 were treated for thyroid cancer without hyperthyroidism, 1 had heart disease without hyperthyroidism, and the rest were considered on clinical grounds to have hyperthyroidism. Fifty patients were followed six months or longer. The remainder had been treated less than six months at the time of the report or were lost to follow-up. Diagnosis was based on the usual laboratory tests for thyroid function, correlated with clinical signs.  $I^{131}$  uptake counts were made before and after therapy. A Geiger-Müller tube was set 19 cm. from the thyroid twenty-four hours after a 0.050 millicurie tracer dose. Most patients were treated in the outpatient department.

Determination of optimum dose was difficult, in that no attempt was made to ablate the thyroid. Attempts were made to calculate the dose by uptake rate, size of gland, and by retained dose. The authors do not feel that complicated time-consuming methods involving considerations of effective half-life contribute much to accuracy. They give a dose which will result in a retention of 0.120 to 0.150 millicurie per estimated gram of thyroid tissue in diffuse toxic goiter and 0.250 to 0.300 millicurie per gram in nodular goiter. Remission was obtained in 79 of 82 cases (96 per cent) followed for two or more months. Forty-eight of 50 cases followed six months showed remission. The total dose for the diffuse goiter cases was from 3 to 29 millicuries, with an average of 10.5, while in nodular goiter the dose was from 9 to 67 millicuries with an average of 29. Of patients receiving less than 10 millicuries initially, one-third failed to show sustained remission. In only about a quarter of those given more than 10 millicuries did transient myxedema develop. Of the 19 with signs of post-treatment myxedema, 14 recovered.

In 1 case of thyrotoxicosis there was a mild flare-up after treatment, and 1 patient complained of tenderness in the region of the gland. Of 29 cases of exophthalmos, 17 were followed six months or more. Seven improved markedly, 4 slightly, and 6 were unchanged. In no instance did exophthalmos develop after therapy.

Failure of a single treatment should not discourage the therapist, especially in nodular goiter. Re-evalua-

tion should be undertaken at two months, six months, and yearly thereafter, with retreatment for recurrence. Regrowth is usually nodular, but a second treatment should follow the pattern for diffuse goiter. Of 3 failures in the authors' series, 1 responded to a second dose and 2 came to surgery. One of the latter had low uptake, probably due to bronchography with Lipiodol shortly before treatment, and the other received too low a dose of  $I^{131}$ . Where antithyrotic drugs are used, they should be discontinued seven days before administration of  $I^{131}$ .

Five tables. GEORGE A. SHIPMAN, M.D.  
New Orleans, La.

**Radioiodine in Treatment of Advanced Heart Disease. End Results in One Hundred Patients.** Henry L. Jaffe, Maurice H. Rosenfeld, Frederick W. Pobirs, and Laurence J. Stuppy. *J.A.M.A.* 151:716-720, Feb. 28, 1953.

One hundred euthyroid patients who were chronically ill and seriously incapacitated with a variety of cardiac diseases were treated with radioactive iodine ( $I^{131}$ ). The rationale of this treatment is that, by lowering the total metabolism of the body, the systemic requirements can be reduced to within the limit of the cardiac reserve. Improvement in associated cardiac symptoms has long been observed following the surgical treatment of hyperthyroidism.

Only patients with the most advanced grade of cardiac disease were accepted for treatment. All other forms of medical treatment had either failed or were inadequate to control symptoms of angina pectoris or congestive failure or both.

The first course of radioiodine therapy consisted of five weekly oral doses of 6 mc. each of radioiodine ( $I^{131}$ ) in 20 c.c. of distilled water. A period of two months was allowed to elapse after the fifth dose, in order to get the full biological effect of the therapy. Since  $I^{131}$  has a physical half-life of eight days, it takes about sixty-four days to get the full physical value of the treatment.

One course of 30 mc. of radioiodine produced myxedema levels or a relative hypothyroid state in 40 per cent of the patients. Two courses of 30 mc., or a total of 60 mc., were necessary to produce a hypothyroid state in 54 per cent of these cases. A total of 90 mc. in three courses of treatment was given to 6 per cent of the patients.



No contraindications to this treatment have been found for properly selected patients. No harmful effects have been observed. No evidence of bone marrow depression, radiation sickness, thyroiditis, or temporary hyperthyroidism has been noted with the multiple small dose technic. The average life expectancy for the entire group has not been decreased and may actually have been increased. A longer period of observation is necessary to evaluate the longevity factor. Of the 24 patients who died as a result of severe cardiac damage, 33 per cent had good symptomatic relief, 25 per cent had fair symptomatic relief, and 42 per cent showed poor response. Therefore, the total end-result study, on a symptomatic basis, shows 61 per cent good results, 26 per cent fair results, and 13 per cent poor results. If the results are scored as poor in the 24 patients who died, then the end-result study shows 53 per cent good results, 20 per cent fair results, and 27 per cent poor results by this method of "medical thyroidectomy." Those favorably affected were relieved of the distressing cardiac symptoms of angina pectoris and congestive heart failure.

Two tables.

ALFRED O. MILLER, M.D.  
Louisville, Ky.

**Intracavitary Colloidal Radiogold in the Treatment of Effusions Caused by Malignant Neoplasms.** Gould A. Andrews, Sam W. Root, Herbert D. Kerman, and Robert R. Bigelow. *Ann. Surg.* 137: 375-381, March 1953.

In patients with inoperable neoplasms involving the peritoneal or pleural surfaces collections of fluid often develop. Radioactive gold ( $Au^{199}$ ) seems a suitable isotope for the treatment of this type of complication.

$Au^{199}$  is a thermal neutron-produced isotope with a half-life of 2.7 days. On disintegration, it produces a beta particle of 0.98 mev and two gamma emissions of 0.12 and 0.41 mev. Its effect in the body is believed to be largely that of beta emission and thus the radiation is localized to the immediate vicinity of the isotope. The gold is administered in the form of a sterile colloidal solution. The optimal dosage is not known; 75 mc. in the chest and 150 mc. in the abdomen are suggested as maximum initial doses.

The patients most suitable for treatment are those who are in relatively good condition, with no important symptoms except those related to fluid. The presence of large masses of neoplastic tissue appears to be an unfavorable sign. A total of 24 cases were treated, including a considerable number which were highly unsuitable for this procedure. In 9 cases, good control of the fluid was obtained. Among the immediate effects of treatment are transitory nausea, vomiting, diarrhea, and bone marrow depression of slight degree. A lag period of a few weeks between administration of the isotope and cessation of fluid formation has been noticed and should be borne in mind before additional isotope is administered.

The authors feel that intracavitary radiogold injection is of distinct palliative value in selected cases. It appears to produce less radiation sickness than conventional roentgen therapy, it is easy to administer, and the unfavorable reactions appear to be minimal. There is little evidence to suggest any benefit from this treatment other than control of fluid and resulting symptomatic relief in selected patients.

Two tables.

SEYMOUR A. KAUFMAN, M.D.  
Boston, Mass.

**Hypoplasia of Bone Marrow Associated with Radioactive Colloidal Gold Therapy.** Thomas W. Botsford, H. Brownell Wheeler, Robert A. Newton, and William E. Jaques. *J.A.M.A.* 151: 788-791, March 7, 1953.

In view of the absence of any reports of serious toxicity associated with clinical use of  $Au^{199}$ , the authors present 4 cases. Of 23 patients treated with colloidal radiogold, 11 received less than 50 mc. and showed no ill side-effects. The white blood counts were not depressed. Three subsequent autopsies from this group revealed normal bone marrow.

Twelve patients received from 58 to 153 mc. of  $Au^{199}$  injected into tumors or body cavities. Six autopsies from this group demonstrated bone marrow depletion and presence of particulate matter consistent with metallic gold. Four of these cases had received no other therapy to account for bone marrow hypoplasia. The detailed protocols of these 4 cases are presented.

It is postulated that particles of the injected radiogold are carried from the injection site to the bone marrow, with resultant depression of marrow elements. In 1 case, focal necrosis and the presence of metallic gold was demonstrated in bone marrow seventy-two hours after intraperitoneal injection.

Eight photomicrographs. JAMES M. SWAIN, M.D.  
Cleveland Clinic

**Lymphatic Drainage Following Intrabronchial Instillation of Silver-Coated Radioactive Gold Colloids in Therapeutic Quantities.** P. F. Hahn and E. L. Carothers. *J. Thoracic Surg.* 25: 265-279, March 1953.

The use of radioactive metallic colloids promises at the present time to become a useful adjunct to surgery in the treatment of bronchogenic tumors in man. Subject to early diagnosis, the treatment of choice in this condition is apparently pneumonectomy, although a few surgeons prefer lobectomy. This procedure, however, is applicable in only approximately one-fourth of all the patients who present themselves for study and diagnosis. Metastasis by way of the lymphatics is the usual course taken. Deep x-ray therapy may increase slightly the time of survival but by many is considered to be of relatively little value except as a palliative agent. It would seem, therefore, that any potentially useful procedure which might be employed in conjunction with pneumonectomy to cut down the propagation of the tumor process should be acceptable, at least from an experimental point of view.

In earlier reports (Meneely *et al.*: *Federation Proc.* 10: 365, 1951) it has been shown that when radioactive gold colloids are administered intratracheally or intrabronchially, a considerable amount of irradiation of the lung parenchyma may be achieved, but since drainage by the thoracic lymphatics was relatively slow, irradiation of the common sites of metastasis was limited. Later it was found that radioactive metallic silver colloids were drained much more rapidly (Hahn *et al.*: *J. Lab. & Clin. Med.* 39: 624, 1952) but difficulties of technical production have obviated their use on a therapeutic scale. In the experiments reported here the distribution of silver-coated radioactive colloid gold particles, following their intrabronchial administration in dogs, was studied at levels of radioactivity which were estimated to be in a therapeutic range for treatment of metastatic lesions in bronchogenic tumors.

A short series of experiments in which the silver coat as well as the gold nucleus was radioactive indicated that the silver coat is gradually leached off in the lung and is carried to the liver for ultimate secretion, probably by the biliary tract.

Silver was found to assist in the transport of the radioactive gold nucleus by way of the lymphatics to the thoracic nodes, thus facilitating irradiation of these common sites of metastatic processes.

Estimated roentgen equivalent dosages to various tissues of interest would suggest that the amount of irradiation to the liver is well within tolerable limits by a factor of perhaps 10 times. Dosages to the lung, into which the material was introduced, are relatively high but this tissue is considered expendable, since in most cases pneumonectomy is planned when treatment is anticipated. Dosages to the lymph nodes are estimated to be of the order of several hundred thousand equivalent beta roentgens. It is felt that discrepancies in uniformity of distribution in such tissues would be well taken care of by the large factor of safety over estimated cancericidal doses necessary to deal with metastatic processes.

Six tables, 1 photomicrograph.

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**Primary Carcinoma of the Mastoid Process. Case Report.** Russell G. Means and John Gersten. *Ann. Otol., Rhin. & Laryng.* 62: 93-100, March 1953.

Cancer primary in the mastoid process and middle ear is extremely infrequent, having been said to constitute 1.5 per cent of all tumors of the ear. It occurs mostly after forty years of age, with equal frequency in males and females, and is extremely rare in Negroes.

The authors report a case in a white male, of fifty-two years, with a history of periods of deafness in the right ear and an accompanying sensation of fullness for the past two years and a half. The middle ear became permanently impaired three months prior to hospital admission, when x-ray studies (October 1951) revealed extensive erosion of the right mastoid bone. No enlarged regional or cervical nodes were palpable. An almost complete paralysis of the facial muscles was present on the right side. At all times the left ear appeared normal.

An extensive radical mastoidectomy was done on Jan. 19, 1952, and the "stem" of the neoplasm was found to have eroded from within through the bony cortex in the upper mastoid region. The pathological diagnosis from frozen sections was "low-grade squamous-cell carcinoma, well differentiated." The operation disclosed that the new growth had intermittently broken down mastoid bone with extensive involvement of the contiguous dura. The wall of the lateral sinus was found to be widely covered with neoplastic growth reaching downward toward the jugular bulb. No metastatic lesions were present. The large subjacent tympano-mastoid cavity was packed loosely with iodoform gauze, preparatory to direct implantation of radiation sources. On the fourth postoperative day a plastic wheel carrying six point sources of cobalt 60 was placed in the cavity, delivering a total radiation dose of about 7,000 r in four days. On the eleventh postoperative day, the tympano-mastoid cavity was closed by suturing the original post-auricular flap in place, after making a large communicating orifice between the external auditory canal and the cavity to facilitate postoperative

care. The patient withstood all of the procedures well. The major postoperative complaints were transitory vertigo with nausea and some nystagmus, all of which gradually subsided.

Follow-up x-ray studies on the seventeenth postoperative day revealed, in addition to an extensive defect of the squamous portion of the temporal bone, extending back to the occipital bone and upward into the parietal area, a further defect of the inner portion and entire tip of the mastoid process down to the middle ear. The patient was discharged from the hospital on the twenty-second postoperative day.

The adjunctive treatment with an artificial radioactive isotope appears to be unique in this situation. No like use of it for this type of case has so far been reported.

Three roentgenograms; 2 photographs; 1 table.

STEPHEN N. TAGER, M.D.  
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**An Improved Iridium-192 Teletherapy Unit.** H. F. Freundlich and J. L. Haybittle. *Acta radiol.* 39: 231-241, March 1953.

The authors investigated the use of iridium 192 in 1949, when large sources of cobalt 60 were not available in Great Britain. A unit which they designed for iridium therapy has been in continuous clinical use at Addenbrooke's Hospital, Cambridge, since May 1950. A rather complete description of the design and the construction of the unit is given, with the method of loading and unloading the isotope so that the operator has rather complete protection (see also Freundlich, Haybittle, and Quick: *Acta radiol.* 34: 115, 1950. *Abst. in Radiology* 56: 919, 1951). Physical measurements are given and the method of overcoming the disadvantages of a half life of seventy-four days is included in the discussions.

The unit described demonstrates the possibilities of using iridium 192 for teletherapy. The mean energy of the gamma rays falls in a most convenient region in that, while being high enough to avoid the disadvantages associated with the selective absorption in bone of normal 220-kv.p. roentgen rays, it is still sufficiently low to make the amount of shielding required small as compared, for example, with cobalt 60. The output of the unit is 23 r/min. at a source-skin distance of 9 cm. and 11.5 r/min. at 13 cm. The problem of increasing the output so that source-skin distances of 25 cm. or more could be used remains.

Mention is made of the use of cesium 137 in a comparable unit and it is felt that an output of 40 r per minute at a source-skin distance of 25 cm. would require 7.5 cm. of uranium shielding to reduce the dose rate at the surface of the head to 0.06 r per hour. Apart from the increase in shielding, the general features of the design of such a machine could be similar to that described for iridium 192. The authors feel that iridium is a possibility for therapy until such a time as large amounts of cesium 137 will be available from Oak Ridge.

Eight illustrations. A. WILSON BROWN, M.D.  
Shreveport, La.

**Behavior of Iodide<sup>131</sup> in Guinea Pigs and of I<sup>131</sup> Rabbit Globulin in Guinea Pigs and Rabbits.** S. P. Masouredis, L. R. Melcher, and Patricia Miller. *Am. J. Physiol.* 172: 565-574, March 1953.

An investigation by the authors revealed that the

behavior of iodide<sup>131</sup> in guinea pigs, as determined by excreta, tissue, and serum radioactivity, is markedly dissimilar to that found after administration of I<sup>131</sup> trace iodinated rabbit globulin in guinea-pigs and rabbits. The rate of loss of I<sup>131</sup> rabbit globulin from the serum after twenty-four hours is 0.68 per cent per hour in the guinea-pig and 0.46 per cent per hour in the rabbit. The rate of loss of radioactivity from the serum of guinea-pigs and rabbits receiving I<sup>131</sup>-labeled rabbit globulin after twenty-four hours is identical to the loss of I<sup>131</sup> from the animal by excretion. Following administration of the I<sup>131</sup> protein, the radioactivity in the liver, kidney, and spleen can be accounted for by the I<sup>131</sup> contained within the plasma of the tissue. No significant cellular localization of radioactivity was found except for the thyroid. After twenty-four hours, the radioactivity administered as an I<sup>131</sup> protein can be quantitatively accounted for by the I<sup>131</sup> in the "globulin" space, thyroid, and excreta.

Three graphs; 4 tables.

**Metabolism of I<sup>131</sup>-labeled Thyroxine—Studies With Isolated, Perfused Rat Liver.** F. N. Briggs, R. W. Brauer, A. Turog, and I. L. Chaikoff. *Am. J. Physiol.* 172: 561-564, March 1953.

I<sup>131</sup>-labeled L-thyroxine of high specific activity was introduced into the perfusate of isolated rat livers, which, under the conditions of the investigation, produced 0.5 ml. or more bile per hour. The injected I<sup>131</sup> appeared rapidly in the bile, obtained from the perfused liver, as much as 20 per cent being excreted in five hours. By filter paper chromatography it was demonstrated that the I<sup>131</sup> in the bile was primarily in the form of a conjugated thyroxine compound, which has been designated Compound U. This compound had previously been shown to be the major excretion product of thyroxine in the bile of the intact rat. The rate of conversion of thyroxine to Compound U by the isolated, perfused liver is adequate to account for the total formation of Compound U in the intact rat. It is concluded, therefore, that the liver is the principal site of this conversion in the normal animal. Rat liver slices, but not rat liver homogenates, showed some activity in converting thyroxine to Compound U. Spleen slices were completely inactive.

Two radioautographs; 1 graph.

**A Comparison of Potassium<sup>42</sup>, Rubidium<sup>86</sup>, and Cesium<sup>134</sup> as Tracers of Potassium in the Study of Cation Metabolism of Human Erythrocytes in Vitro.** William D. Love and George E. Burch. *J. Lab. & Clin. Med.* 41: 351-362, March 1953.

The studies of potassium metabolism of human erythrocytes as described in this report were undertaken in order to observe cellular electrolyte metabolism of man under controlled *in vitro* conditions. The usefulness, for this purpose, of Rb<sup>86</sup> and Cs<sup>134</sup> as compared with K<sup>42</sup> was investigated. Since rubidium and cesium belong to the same group of elements as potassium and resemble the latter in many of their biological properties, it was believed that their metabolism might also be similar and that their longer half-life (19.5 days for Rb<sup>86</sup> and 2.3 years for Cs<sup>134</sup>) might make them useful for long-term experiments for which the short-lived K<sup>42</sup> (half-life 12.4 hours) is unsuitable. The blood used for the experiments was obtained from laboratory personnel and in two instances from patients with congestive heart failure.

Observations were made on (1) the partition of each of the elements studied between the red cells and plasma after final stable distribution of the tracer had been nearly reached; (2) the rapidity with which final levels were approached; (3) the effects of temperature change on the potassium exchange rate; (4) the effect of changes in the plasma potassium and rubidium level on the rate of disappearance of the isotopes used from the plasma.

The eventual quantitative partition of the three isotopes between erythrocytes and plasma, after they were added to the plasma, was found to be nearly the same. Calculated exchange rates of potassium between erythrocytes and plasma were not detectably different with K<sup>42</sup> or Rb<sup>86</sup> as the tracer. The mean exchange rate as measured by Rb<sup>86</sup> was 2.1 per cent of the red cell potassium per hour; the figure for Cs<sup>134</sup> was less than one-fifth as great. The effect of changes in the temperature of incubation and of raising the plasma potassium concentration was the same for each isotope.

The results suggest that Rb<sup>86</sup>, with its half-life of 19.5 days, may be useful under some circumstances as a tracer for potassium, at least from a qualitative point of view. Pertinent data should be validated with K<sup>42</sup> wherever possible.

Two graphs; 3 tables.

**The Fate and Pathologic Effects of Plutonium Metal Implanted Into Rabbits and Rats.** Hermann Lisco and Walter E. Kisielski. *Am. J. Path.* 29: 305-321, March-April 1953.

Pieces of plutonium, <sup>239</sup>Pu, ranging in weight from 0.61 to 1.80 mg. were implanted subcutaneously in 8 male rabbits and 3 female rats and examinations were made at regular periods thereafter both by palpation and roentgenographically. The animals were sacrificed when moribund, and retention and organ distribution studies were carried out.

Roentgenograms obtained two weeks after implantation showed that the solid pieces of metal had broken into minute fragments and these were dispersed over a small area. In the rabbits, subsequent examinations showed the persistence of some granules until death, but it was not possible to trace any one fragment through a series of films, since changes were continuous. Concomitant with fragmentation there developed a localized and, in some instances, a gradually increasing soft-tissue density, producing a shadow outlining the site of implantation. The implantation sites became heavily calcified in all animals.

Despite fragmentation of the metal, only a small fraction of it was found to be actually absorbed and distributed throughout the bodies of the animals during an observation period of 1,048 days.

Retention and organ distribution studies gave evidence that rabbits absorbed considerably more plutonium under the conditions of the experiment than rats. The majority of the animals appeared to suffer no ill effects from the local implants or from the absorbed plutonium. One rat, however, died with an osteogenic sarcoma of the spine produced by the deposition of plutonium in the skeletal tissues. The data indicate that both species can harbor considerable quantities of unmetabolized plutonium in the subcutaneous tissues without showing evidence of this in the excreta.

Ten roentgenograms; 4 photographs; 1 photomicrograph; 3 tables.

**In Vitro Studies of Aspects of the Metabolism of Sodium by Human Erythrocytes Using Sodium.** William D. Love and George E. Burch. *J. Lab. & Clin. Med.* 41: 337-350, March 1953.

Erythrocytes readily lend themselves to *in vitro* study of certain aspects of the basic processes and principles of cellular sodium metabolism, since they can be removed from the body and maintained under satisfactory conditions. Their content of sodium and potassium approximates that of human cells in general, and the maintenance of a low sodium and high potassium level involves active cellular metabolism.

This report is concerned with a study of the sodium within the red cells of a small group of human subjects. The total intracellular sodium was measured by a flame photometer, and the amount of rapidly exchanging red cell sodium was determined by adding  $\text{Na}^{22}$  to the plasma and following the rise in red cell radioactivity until it reached a plateau value, usually after four to six hours.

In the majority of the experiments, substantially all of the red cell sodium was found to exchange at a uniform and rapid rate with the plasma. In one subject, however, with a relatively high total red cell sodium, there remained a portion of the sodium which had not exchanged with the plasma sodium at six hours, indicating that sodium may exist within the red cells in a "bound" state. A mean of 3.7 mEq. of sodium entered a liter of red cells in one hour. This was 64 per cent of the rapidly exchanging sodium content of the cells.

Reducing the temperature at which the blood was incubated, from 38 to 28°C., resulted in a more than 50 per cent decrease in the exchange rate. Six drugs—epinephrine, neostigmine, lanatoside, pitressin, cortisone, and DOCA<sup>21-22</sup>—produced no striking effects on the sodium metabolism.

The *in vitro* system provided in studies of this sort gives an opportunity to measure the effects on cellular sodium metabolism of various drugs and chemicals of known clinical importance. In addition, it is possible to remove from man, both healthy and diseased, a living cellular system for analysis *in vitro*, thus facilitating a study of possible abnormalities of cell electrolyte metabolism characteristic of disease.

Four graphs; 3 tables.

**Erythrocyte Life Span in Small Animals. Comparison of Two Methods Employing Radioiron.** E. Langdon Burwell, Barbara A. Brickley, and Clement A. Finch. *Am. J. Physiol.* 172: 718-724, March 1953.

By employing radioiron-tagged erythrocytes, the life span of rabbit, rat, and mouse cells was determined. The average survival of the rabbit erythrocyte was found to be forty-five to fifty days, the rat erythrocyte forty-five to fifty days, and the mouse erythrocyte twenty to thirty days. Random cell destruction occurred in all species. Estimation of red cell life span in rabbits by the serum iron turnover-red cell utilization technic gave significantly lower values.

One diagram; 3 graphs; 1 table.

## RADIATION EFFECTS

**Roentgen-Ray Cataract. Effects of Shielding of the Lens and Ciliary Body.** A. J. Alter and P. J. Leinfelder. *Arch. Ophth.* 49: 257-260, March 1953.

The occurrence of cataract following exposure of the lens to ionizing radiations has been demonstrated in both man and experimental animals. Most observers consider the injury to occur primarily in the lens, as a result of direct damage either to the epithelium or to the lens fibers and their proteins. The nature of this change has been thought to be an alteration in the chemical, enzymatic, physical, or cellular processes of the lens, occurring as a direct result of irradiation. Others believe that the lens damage is indirect, caused by the impaired nutrition that results from injury to the blood vessels of the ciliary body. In order to test the validity of these hypotheses, the authors devised experiments so that either the ciliary body or the lens could be selectively submitted to a cataractogenic dose of roentgen rays.

Five lead shields 2 mm. in thickness were employed to protect certain portions of the lens or the eye from direct irradiation, and to exclude, so far as possible, other structures. In each experiment one of these shields was sewed to the sclera of one eye of young albino rabbits, under pentobarbital anesthesia. The shielded eye was then exposed in a direction perpendicular to the cornea to a coned beam of roentgen rays (120 kv., 26 cm. distance; half-value layer, 3 mm. Al). One thousand roentgens in air, an amount estimated to be cataractogenic, was the routine experimental dose. In a few instances a larger dose was given.

These experiments again demonstrated the relation

of roentgen radiation to cataract and, in addition, indicated the direct association of exposure of the lens to the development of lens opacities. When the lens was protected from radiation, no cataract occurred, even though the ciliary body received a dose sufficient to produce cataractous changes. The experiments also showed the more actively growing portion of the lens, the lens epithelium and fibers of the equatorial region, to be especially sensitive; exposure of this region yields the same results as irradiation of the entire lens. The more central segment of the lens is relatively insensitive, and twice the dose that produces cataract on exposure of the peripheral portion is ineffective centrally.

Exposure of one quadrant of the lens to roentgen rays resulted in opacities limited to that quadrant.

In most instances the shields did not protect the opposite eye, and cataract occurred because of direct injury by the radiation. The occurrence of cataract in the opposite eye thus acted as a positive control of the cataractogenic character of the radiation used.

One illustration in color; 1 drawing; 1 table.

**Developmental Defects Following Irradiation of the Ovaries in a Child.** U. V. Portmann and E. Perry McCullagh. *J.A.M.A.* 151: 736-739, Feb. 28, 1953.

In 1934, a 15-month-old girl was operated upon for a slowly enlarging tumor of the abdomen known to have been present for two months. At operation, a tumor about 10 cm. in diameter was found, firmly attached to the bifurcation of the aorta. It could not be removed. All other organs were normal. Biopsy was interpreted



as revealing an ependymoma. Recent review of the slides, however, indicated the tumor to be a neuroblastoma.

Following operation, roentgen therapy was administered to anterior and posterior pelvic portals with fields 10 X 10 cm. Approximately 800 r was delivered at the level of the tumor and ovaries. Three months later, the child had gained in weight and appeared normal. The tumor had regressed to about one-half its original size. A second course of therapy was then given, approximately 500 r being delivered to the level of the tumor and ovaries. Following this the tumor could no longer be felt.

The patient was followed periodically and seemed to progress normally as a child but was small for her age. At the age of seventeen she had not menstruated. At that time her height was 59 1/2 in.; weight, 84 1/2 lb.; blood pressure, 154/100. Muscular development was good for her small stature. The breasts were pre-adolescent, without pigmentation of the nipples. The abdominal and pelvic anatomy was small in proportion to the rest of her body. A few fine axillary and pubic hairs were present, but the external genitalia and uterus were infantile. There was no evidence of a pelvic tumor.

Of the many laboratory studies performed, the following are of interest: urea clearance, 75 per cent of normal the first hour, 71 per cent the second hour; urinalysis, normal; vaginal smear, typical castrate type. Urinary gonadotrophin levels were more than 105 and less than 212 mouse units per twenty-four hours (normal, 6 and 50). This assay is entirely consistent with the idea that ovarian failure was primary, resulting in pituitary hyperactivity.

A diagnosis of hypo-ovarianism due to irradiation of the ovaries in infancy was made, based on the physical examination and the excess of pituitary gonadotrophin. Estrogen therapy was begun. Diethylstilbestrol was given orally in a dose of 5 mg. per day. After four months some breast development was visible and axillary and pubic hair appeared. The dose of diethylstilbestrol was increased to 10 mg. per day and after an additional six months of this therapy the patient's height was 60 1/2 in. At the time of the report she was 18 years and 5 months of age and skeletal maturity was about that of a normal 18-year-old girl. Breast development was judged to be normal for a girl of thirteen. Since later progress appeared to be somewhat slow, an attempt to develop a more normal response, including glandular breast development, was made by adding progesterone to the estrogen therapy. After three months of this therapy further breast growth was evident. Treatment was withheld for a few days after each course of four injections of progesterone, and artificial menstrual bleeding was produced regularly.

One roentgenogram; 2 photographs; 1 photomicrograph.

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**Hematologic Studies of Irradiated Survivors in Hiroshima, Japan.** Yoshimichi Yamasawa. Arch. Int. Med. 91: 310-314, March 1953.

The author reports a hematologic survey conducted from March 1948 to February 1949, on 824 irradiated residents of Hiroshima, thirty-three to forty-four months after the detonation of the atomic bomb. The findings in this group are compared with those in a

control group of 1,145 residents of Kure. Results of the initial hematologic studies on 304 of the irradiated individuals were presented in 1949 (Snell, Neel, and Ishibashi: Arch. Int. Med. 84: 569, 1949. Abst. in Radiology 55: 640, 1950).

Although statistical differences are apparent in the two groups, when one takes into account errors inherent in the hematologic methods themselves and differences in the possible incidence of parasitism and nutrition, it would be unwarranted to attribute the slight changes found to the effects of irradiation.

The data obtained in the survey seem to indicate that irradiation resulting from the explosion of the atomic bomb in Hiroshima, on Aug. 6, 1945, has not significantly altered the hematologic values, as analyzed in this report, over a three- to four-year period.

Two tables.

**The Treatment of Radiation Pneumonitis with Cortisone.** Sanford G. Bluestein and Jacob Roemer. J. M. Soc. New Jersey 50: 106-107, March 1953.

The authors report a case of radiation pneumonitis treated with cortisone in a 45-year-old white woman with no previous carcinoma, arteriosclerosis, or infection in the lungs. The patient had a left radical mastectomy for carcinoma with left axillary node involvement. A skin nodule on the right side prompted radiation therapy for sixty days. Sudden onset of severe cough and dyspnea and roentgen demonstration of apical infiltration consistent with radiation pneumonitis led to the immediate administration of cortisone and penicillin. Symptoms lessened within twenty-four hours and disappeared completely in one week. The cortisone dosage was 100 mg. daily for the first week, 50 mg. daily for the second week, and 25 mg. daily for the third week.

A recurrence of the cough at the end of one month responded to a similar dosage of cortisone. The length of follow-up is not stated, although the patient was well at the time the article was written. A film after one month showed complete resolution of infiltration on the right but no change on the left; at three months the chest film was normal.

The authors conclude that therapy should be maintained at high levels for at least four weeks and continued for at least six to eight weeks.

Three roentgenograms. JOHN J. CRAVEN, M.D.  
Cleveland Clinic

**Effects of Middlethal Doses of Total Body Ionizing Radiations.** Elbert DeCoursey. J.A.M.A. 151: 904-905, March 14, 1953.

The effects, on tissues, of ionizing radiations of all types, including nuclear particles, gamma and roentgen rays, are briefly considered. Our present knowledge of radiation effects depends largely upon experience with focal area therapy. This differs essentially from total-body irradiation. In the former, the small volume of tissue exposed, slow rate of absorption with divided doses, and relative radioresistance of adjacent tissues in many areas, all permit higher doses. In the latter, every tissue is potentially affected, and consideration of each in order of decreasing radiosensitivity is mandatory.

The total-body effect is proportional to the individual sensitivities of the different tissues and to the amount of radiation they absorb, so that the whole organism is

only as resistant as the most sensitive organs. In order of decreasing sensitivity these are: the hematopoietic system, including the bone marrow and lymphoid tissues; intestinal glands; gonadal epithelium; the skin and lens epithelium; endothelium; fibrous tissues; interval epithelial organs; cartilage and bone; muscle; neural tissue.

The total-body effect is produced largely by acute radiation injury to (a) bone marrow and lymphoid elements, as evidenced by hemorrhage, infection with organisms ordinarily non-pathogenic, and inflammatory processes, including leukopenic ulceration and necrosis of the external and internal body linings, and (b) intestinal mucosa, as evidenced by early gastrointestinal symptoms. Thus approximately mid-lethal doses of total-body ionizing radiation result mainly in aplastic anemia combined with gastrointestinal injury.

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**Prophylactic Antibiotic Therapy in X-Irradiated Animals.** Willie W. Smith, Falconer Smith, H. Jeanette Ruth, Harry Y. Canter, and Marie M. Grenan. *Am. J. Physiol.* 172: 351-358, February 1953.

In the present paper the authors report a study of the efficacy of prophylactic antibiotic treatment in irradiated mice, rats, and guinea-pigs. In the two papers which follow (see succeeding abstracts) they describe an investigation of the occurrence and identity of infecting organisms and their relation to survival time in treated and untreated mice, and the response of irradiated mice, with and without antibiotic treatment, to some experimentally induced infections.

Mice used in the investigations were from an inbred NIH strain. One or more litters, at the age of seven weeks, were caged together for two weeks, at the end of which time each mouse was given a separate cage. A week later the animals were irradiated in groups of 10. Litters and irradiation groups were distributed as equally as possible among the antibiotic-treated groups, which usually consisted of 30 or more animals. One or more of these groups served as irradiated controls. Radiation factors were 200 kv., 20 ma., 0.51 mm. Al and 0.25 mm. Cu added filtration, and 20 cm. target distance. The usual dose was 625 r. Approximately half of the weaning batches of mice that were studied over a period of sixteen months showed favorable survival results with Streptomycin. With few exceptions, the Streptomycin was administered only following irradiation. Other antibiotics used in combination with Streptomycin in no instance significantly improved the Streptomycin result and usually the effect was less favorable than with Streptomycin by itself.

Sprague-Dawley weanling male rats were given individual cages, and one week later were irradiated in a partitioned Presdwood box in groups of 12, with all antibiotic-treated groups represented as equally as possible. Diet and irradiation factors were the same as in the experiments with mice except that target distance was 75 cm. and the air dose in each experiment was 750 r. The mean time to death was prolonged in several of the groups given Streptomycin or Terramycin, although percentage survival was in no case significantly increased. Penicillin was without significant effect in three groups where the dose was 15 or 20 mg./kg. body weight, but the animals in one group

given 20, and in another given 30 mg./kg. died earlier than their controls. The incidence of diarrhea was significantly reduced in the groups treated with Streptomycin or Terramycin but not among animals receiving penicillin.

At the age of about five weeks, 47 male and 48 female guinea-pigs were given 350 r, irradiation factors being the same as for the rats. Streptomycin was given in subcutaneous injections of 75 mg./kg. body weight twice a day from the first through the fourteenth day following irradiation to 24 males and 24 females. Of the untreated controls 83 per cent, and of the streptomycin-treated animals 69 per cent had died by the twenty-eighth day, a difference not considered significant.

From a practical point of view it would be very useful to extrapolate these results to man, but the authors feel that an attempt to predict the value of universal prophylactic treatment after irradiation uncomplicated by burns or other injury would be unwarranted on the basis of their experience with experimental animals, or that of others reported in the literature.

Six tables.

**Naturally Occurring Infections in Untreated and Streptomycin-Treated X-Irradiated Mice.** Leon Gonschery, Robert Q. Marston, and Willie W. Smith. *Am. J. Physiol.* 172: 359-364, February 1953.

In the present experiments, which are a continuation of the investigation described in the preceding abstract, the authors studied the incidence and identity of bacteria found in heart blood and spleen of mice dying following 1,400 to 550 r, the relationship of these infections to survival time, and the influence of Streptomycin treatment on the incidence and type of infection found at death following 625 r.

In the first experiment a single weanling batch of 489 mice were divided into six groups, balanced as to litter, and irradiated with doses ranging from 1,400 to 550 r. In the four succeeding experiments animals comprising two balanced groups totaling 446 mice each were irradiated with 625 r; in one of the groups each animal was given a daily subcutaneous injection of 5 mg. Streptomycin sulfate from the third through the twenty-eighth day following irradiation. All of the mice were males of the inbred NIH strain, caged separately and irradiated at the age of seven to eight weeks as previously reported. Heart blood was obtained by aseptically opening the chest and puncturing the heart with a capillary pipette.

Evidence of the influence of infection on lethality following irradiation was demonstrated in a shortening of the survival time of animals showing certain types of infection at death. Deleting the animals that showed positive cultures at death resulted in an essentially linear relationship between dose and time to death in the dose range 800 to 550 r. Infections were rarely observed in mice that died about three and a half days after irradiation (1,400 and 1,100 r) and were most frequently observed in animals that died after six to nine days, with the incidence reduced in those that died in the third week following irradiation. With Streptomycin treatment, although there was not always a significant reduction in mortality, there was always a reduction in the number that showed positive blood cultures and an increase in those showing negative

cultures at death. Streptomycin treatment resulted in a prolongation of survival time which was independent of the presence of organisms in the blood at death.

Three graphs; 4 tables.

**Experimental Infection and Streptomycin Treatment in Irradiated Mice.** Robert Q. Marston, Leon Gonschery, Ilo M. Alderman, and Willie W. Smith. *Am. J. Physiol.* 172: 365-371, February 1953.

The investigation described here is a continuation of the experiments outlined in the two previous abstracts.

Bacteriologic studies of infections observed in irradiated mice have raised three major questions: (a) Is the presence of the organism isolated a causative factor in the death of the irradiated animal? (b) What is the pathogenic significance of the drug-sensitive organisms isolated from the antibiotic-treated animal? (c) What is the basis of the variation observed in the effect of prophylactic antibiotic treatment of irradiated animals? Experimental infections, though in many respects not comparable to natural infections, are useful in clarifying some of these problems and in studying the functional aspects of the defense mechanism after irradiation.

In most of the experiments the radiation dose was set at a low lethal level (475 r, 28-day mortality 8 per cent) and three days later the mice were inoculated subcutaneously with doses of organisms which were essentially non-fatal to mice. Radiation factors and cultural procedures were the same as in the experiments described in the two preceding papers. Streptomycin sulfate was administered subcutaneously in 0.2 ml. of saline. With the exception of one experiment, the first dose was given six hours and succeeding doses at intervals of twenty-four hours after inoculation.

Of the eight organisms tested, all but two strains of *α-Streptococcus* (H and M) resulted in increased mortality in mice irradiated with 475 r. Streptomycin was effective with *Staph. aureus*, partially effective with *Paracolon*, *E. coli*, and *Proteus* (Kf; and M) and ineffective with *Pseudomonas* infections. With *Proteus* Kf, Streptomycin reduced mortality only during the first two days after infection, although in both early and late periods there was a reduction in the incidence of positive and an increase in negative blood cultures. Treatment for three days with 1.25 mg. of Streptomycin per day was almost as effective in reducing mortality (though not as effective in reducing the incidence of positive blood cultures) as longer treatment with 2.5 or 5 mg. twice a day. Susceptibility to *Proteus* showed no further increase, nor did the efficacy of Streptomycin show a decrease, from the third through the twelfth day after irradiation with 475 r. After a radiation dose as low as 250 r the animal still showed marked susceptibility to *Proteus* infection. Streptomycin was more effective at 250 r than at 475 r.

Two graphs; 6 tables.

**Effects of Total Body X-Irradiation on the Peripheral Blood of the Monkey.** Earl Eldred and Bergliot Eldred. *Blood* 8: 262-269, March 1953.

Nine healthy monkeys were exposed to single doses of whole-body irradiation of 550 to 700 r. The peripheral blood was then studied at intervals up to eight months. In general, the changes were similar to those found in other animals, consisting of an initial fall in the number of circulating leukocytes, a period of sustained depression, and a subsequent return to normal.

The total white counts made one to five hours after irradiation showed an increase over the pre-irradiation range. This increase was due entirely to a rise in the neutrophil level. It was noted during this time that the band forms increased up to 10 per cent of the total cells (pre-irradiation average of 2 per cent). During the next few days there was rapid drop in total count, down to a 100 to 750 range in the 3 animals that died. Thirty-three days after the irradiation the white blood count of each survivor had returned to the pre-irradiation level.

Eosinophils were present for three days after irradiation at 600 to 700 r, but then were virtually absent from the fourth to the twenty-seventh days. An eosinophilia followed during the fifth to the seventh week after irradiation.

Lymphocytes began decreasing in number immediately after irradiation, but the depression was never as great as with the neutrophils, and for a period of two weeks most of the cells seen were lymphocytes. Monocytes disappeared entirely by the fourth post-irradiation day but became plentiful during the third week, when they averaged 22 per cent of the differential count. The platelets decreased slowly in number for the first seven days after irradiation but then dropped rapidly. By the third week, however, the platelets in the survivors were as plentiful as before irradiation.

The erythrocytes declined slowly during the first week. Their lowest levels were reached in the second to third week, after which they began to increase slowly.

Three graphs; 1 table.

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**Experimental Studies on the Effect of Ionizing Radiation Delivered Intermittently.** Ernst Witte. *Strahlentherapie* 89: 586-591, 1953.

The author examined the effect of intermittent ionizing radiation on *Drosophila* eggs and larvae. For the larvae, a very marked effect was found with single exposure times of less than one second. A statistically significant minimum was established for an exposure time between  $10^{-4}$  and  $1.4 \times 10^{-3}$  seconds, which is about 60 per cent of the value for continuous irradiation. The effect was independent of the relation of exposure time to the interval between exposures, which varied between 1:9 and 1:2. Studies with *Drosophila* eggs did not show any significant effect for the same experimental conditions.

Eight illustrations. ULRICH K. HENSCHKE, M.D.  
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**Effects of Total Body Irradiation Upon Lipoprotein Metabolism.** John E. Hewitt, Thomas L. Hayes, John W. Gofman, Hardin B. Jones, and Frank T. Pierce. *Am. J. Physiol.* 172: 579-587, March 1953.

Lipoprotein concentrations were determined in 49 adult white rabbits following total-body irradiation with doses ranging from 800 to 900 r. Irradiation factors were 220 kv., 0.5 mm. Cu filtration, target distance 60 cm., 40 r per minute to center of animal.

An excellent correlation was found between high level of total lipoprotein thirty hours after irradiation and subsequent death of the animal. A serum opalescence was associated with low-density lipoprotein only, not with total lipoprotein. Changes in the lipoprotein

levels after irradiation were consistent with the theory of conversion of low-density lipoprotein to higher density components. The injection of heparin after irradiation hastened the return of lipoprotein levels to normal values. The injection of toluidine blue produced changes in the lipoprotein pattern similar to those shown after irradiation.

Three illustrations; 2 tables.

**Roentgen Rays and Wound Healing. An Experimental Study.** Walter Lawrence, Jr., James J. Nickson, and Lesley M. Warshaw. *Surgery* 33: 376-384, March 1953.

Young rats were subjected to standard abdominal incisions, comparable to clinical laparotomy incisions, immediately following irradiation of the wound area and at intervals up to three months thereafter. Physical factors were 100 kv., 6 ma., 1 mm. Al filter, half-value layer 18 mm. Al, 15 cm. target-skin distance. Since measurements of abdominal wall thickness all fell between 2 and 3 mm., depth dose calculations revealed that the peritoneum received a dose 96 per cent of the air dose (2,000 r), i.e., 1,920 r. Studies of the rate of healing of the wounds in terms of tensile strength showed that all wounds reached the maximal strength range, although there was some delay in the rate of attainment of this strength by the irradiated wounds. Delay in healing was most marked in wounds receiving irradiation immediately or one week before surgery. The difference in the healing curves between tissues irradiated three weeks, five weeks, eight weeks, and twelve weeks prior to surgery was not great. Nutritional and histologic studies confirmed the data obtained in the measurement of tensile strength of the healing wounds.

These data suggest that healing of surgical wounds in recently irradiated tissue is impaired, in a practical sense, only in terms of rate of healing and not in terms of final wound strength. The data also seem to demonstrate little or no practical advantage in delaying surgery more than three weeks after irradiation. The presence or absence of irradiation-induced skin erythema, *per se*, seems to have little effect on the rate of wound healing in the rat.

One graph; 1 table.

**Influence of Homologous Tissue Factors on DNA Turnover and Radiation Protection.** Lola S. Kelly and Hardin B. Jones. *Am. J. Physiol.* 172: 575-578, March 1953.

The authors cite from the literature a number of studies indicating that DNA (desoxypentose nucleic acid) formation in the tissues is depressed by irradiation and enhanced by the presence in an animal of growing tissue (tumor or embryo). Experiments are now presented which indicate that substances capable of stimulating DNA formation can be obtained from mashes and extracts of rapidly growing tissues and that these substances may offer some protection after exposure to radiation. The explanation suggested is that rapidly dividing cells release an active substance into the circulation which stimulates other cells to divide and that this same substance or a similar one exists in tissue mashes.

Special attention was given to the specific activities of the liver and spleen DNA. The activities of liver DNA were found to be higher in the animals which re-

ceived embryo mash compared to the controls, while the spleen DNA values did not show a difference until the seventh day post-irradiation. Experiments are in progress now to determine if tissues such as bone marrow and lymph nodes, which show severe irradiation damage, are also helped toward recovery by embryo mash or other tissue mash injections.

Two tables.

**Effect of X-Rays on Trichina Larvae.** S. E. Gould, James G. Van Dyke, and Henry J. Gomberg. *Am. J. Path.* 29: 323-337, March-April 1953.

The authors report a study of the effect of irradiation on *Trichina* larvae *in vitro*. The larvae were obtained by digestion of muscle of white rats that had been infected two to four months previously. The radiation factors were 200 kv., 20 to 25 ma., with inherent filtration of about 0.15 mm. Cu. In all experiments a Victoreen rate meter was used to indicate the x-ray output, which was held constant for any given experiment by varying the emission of the tube filament. The calibration standard was a Victoreen condenser r meter. For the high dose rates employed, a 2,500 r chamber was used. With filtration by 0.5 mm. Cu plus 1 mm. Al, the rate was of the order of 1,000 r per minute.

It was found that a dose of 750,000 r caused death of all or nearly all larvae within one to two hours after irradiation. Reproduction of *Trichinae* was largely prevented by exposure to 3,500 r and maturation to adult forms by exposure to 5,000 or 6,000 r.

Pieces of trichinous meat in thicknesses of 1.45 cm. were rendered non-infective to experimental rats when the meat was exposed to 15,000 r. This suggests that the dose of irradiation required to sterilize *Trichina* larvae in commercial quantities of pork may not be excessive.

Four photographs; 2 photomicrographs; 4 tables.

**Detection of Cosmic Radiation by Chemical Methods.** J. Eugster. *Radiol. clin.* 22: 130-139, March 1953. (In German)

Several dyestuffs are sensitive to x-radiation. Methylene blue and phenol-indo-2,6-dichlorophenol are both decolorized, while the Folin phenol reagent becomes colored. An acidity reaction to short wavelength radiation occurs in water saturated with chloroform. When one part of water containing between 9 and 30 per cent brom-cresol purple as an indicator is overlaid with fifteen parts of chloroform and then irradiated, the pH decreases, the solution becomes more acid, and the indicator changes from red to yellow. This chloroform acidity reaction can be set up to measure fixed quantities of radiation, such as 200, 400, or 600 r with an accuracy of within 5 r.

A recent development is the vital stain TTC or 2,3,5-triphenyl-tetrazolium chloride (Bingham and Company, New York, N. Y.). TTC is colorless and water-soluble but upon irradiation reacts chemically with ionic hydrogen to yield triphenyl formazan, which is red and insoluble. With the sensitivity greatest in the ultraviolet region, one must not be misled by the theoretic low sensitivity to gamma radiation, because the reaction is also activated by corpuscular emission whether primary or secondary.

The loss in activity of certain enzymes upon irradiation, particularly phosphoglyceraldehyde-dehydro-



genase, myosin, succinoxidase, and hexokinase, is striking. Determinations of the order of 1 r have been reported.

It would seem at first glance that these chemical methods would be too gross to detect cosmic rays. Further consideration shows, however, that cosmic rays cannot be compared with x-rays or gamma rays in terms of roentgens. The effect of high-energy quanta, when evidenced as secondary corpuscular emission, is one of tremendous ionization. The author's experiments began with exposure of methylene blue plates for sixty-one days at an altitude of 3,500 meters on the Jungfrau. Star figures indicative of cosmic ray impacts were clearly demonstrable. Similar effects were obtained with the Folin phenol reagent. Following this, in January of 1952, a plexiglass plate with 70 small

plaques of emulsion containing TTC was exposed on the Jungfrau. Not only were the changes as seen with cosmic radiation demonstrable but also larger star figures, as from bombardment with high-energy protons, were noted. Further exposures of TTC-impregnated emulsions to an altitude of 28,000 meters have clearly shown the presence of heavy primaries, presumably hydrogen nuclei. The experiments are being continued, using TTC, hormones, enzymes, and living tissue. Anent this last mentioned material, two of the illustrations are rather intriguing: an ionization track of cosmic origin in TTC impregnated human skin and a star figure of similar origin in human omentum.

Four illustrations, one in color.

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